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# BRITISH MEDICAL JOURNAL

JOURNAL OF THE BRITISH MEDICAL ASSOCIATION

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BRITISH MEDICAL JOURNAL

LONDON SATURDAY AUGUST 27 1949

# GOETHE, AN APPRECIATION

BY

Sir CHARLES SHERRINGTON, O.M., G.B.E., F.R.C.P., F.R.S.

A cultivated public our civilized world over is now celebrating the bicentenary of the birth of Johann Wolfgang von Goethe. It would be difficult to find a happier event for commemoration. It had become Germany's turn for a literary heritage. America was still a stripling; the East was for Europe still a region partly fabulous. Our own continent rang the changes on itself. In *belles lettres* France and ourselves divided the honours. In our own case an era had supervened when the heroic couplet was supreme; even Homer's rush and flow were subject to it by the skill of Alexander Pope; and Thomson's *Seasons* offered a rural counterpoise to it with a commanding Continental following. Then it was that the German tongue in literature began to be heard—Herder, Schiller, and, as its head and front, Goethe.

Looking back in 1824, Goethe wrote, "I was fortunate. Shakespeare had left in English nothing else to do; but in German I soon got in front of what there was." The new era hailed not from Vienna or Berlin but from a provincial Court, Saxe-Weimar. It brought an engaging air of freshness; it derived from native springs. In some respects it had cousinship with ourselves, Burns, and the Percy *Reliques*. As an invasion it was transient, but its result was lasting. It affected Coleridge but touched little if at all the Romantics—Keats and Shelley and Wordsworth. Byron did not react to it, though it reacted to him. Its influence, of course, had in foreign travel to meet the drawback of using an alien tongue, and that difficulty was enhanced by a further circumstance—that the spear-head of the invasion came in the form of the lyric, and the great lyric is especially refractory to translation. It is often in short lines employing rhyme and a condensed felicity which must yet be simple. As examples, and taking recourse to memory and to comparison, "Wer nie sein Brot mit Thränen ass," runs with "Fear no more the heat o' the sun"; and then again, "Liebchen, kommen diese Lieder jemals wieder dir zu Hand?" runs with "Who is Sylvia, what is she?" or de Musset's "Elle était belle, si la Nuit." The word-music is so wedded to the sense that no other words will do. Its audience is limited therefore to a native audience consisting of those to whom its language is their home tongue, and to a relative few outside that circle. Shakespeare's songs illustrate this and so do Goethe's *Gedichte*. Their native magic is incomparable, but it is not for export. This is a strong plea for a common language. The old monkish chants were in Latin. Esperanto? No, no; not until Esperanto has been lived in, laughed in, wept in, rejoiced in, sobbed in, can it be an adequate vehicle for a great lyric. Will such a day ever dawn?

Of all the major works of Goethe, I should suppose the dramatic poem, *Faust*, Part I, is the one most read to-day. I once visited the exceptionally complete Goethe library at Yale, and an impression which I received there was that of all his works *Faust*, Part I, is that which has called for most editions. It suffers somewhat less as to width of audience from the translation difficulty than do the lyrics. The story's general outline is so well known that even a reader not fully skilled in German can open it practically at any page and pick up something of the beauty of the text. We in English have the added zest of the echo of Marlowe's *Faustus*: "Was this the face that launch'd a thousand ships, and burnt the topless towers of Ilium? Sweet Helen, make me immortal with a kiss!" As imaginative poetry those lines are scarcely to be excelled, but Goethe's *Faust* is far richer in sustained intellectual dialectic. It is a poem in drama rather than an acting play; it is, however, given on the stage, especially in Germany, where it has the added appeal of being German. In it Goethe is thought to have succeeded in characterization better than anywhere else in the young girl Gretchen of Part I. Perhaps it is a pity that we readers should be asked to find a continuation of her in the somewhat wearisome Helen of Troy of Part II. Goethe is at his weakest in this respect in Part II. Of course he was when composing Part II already an aged man. As to the other *personae* of Part I, the restraint exercised in the delineation of Mephisto is a notable inspiration, a sort of mischievous "God's ape," too aloof for delight in the cruelty of what he does—a rebel against heaven, but of the meaner class. Anything more remote from Milton's Satan is not to be conceived. *Faust*, Part I, also instances what is not frequent in Goethe, humour—the garden scene with Martha.

As we think back to Goethe's masterpieces they strike us by their variety. During much of his career he was a literary sounding-board for the Europe of his time. *The Sorrows of Werther* is a case in point. It has, I suppose, passed over into unreadability. But a romance which once took the reading world by storm cannot be altogether devoid of lasting merit. It reflected wholesale the sentimentality of a period when society lived on the brink of war, when domesticity in woman was a universally admired virtue and middle-class domesticity yearned for the romance attaching to the class above it. Sentimental romance is sadly at the mercy of satire, even from the good-natured. In halcyon times which we now call Victorian, Thackeray rallied the dear high-waistcoated Charlotte of Goethe. He remarked that even after her lover had killed himself "she, like a well-conducted person, went on cutting bread-and-butter." Goethe in his later years said that in Werther he was like the pelican drawing blood from his own breast. Is there not a Werther period in most young men, even to-day?

Then there is *Iphigenia*, a statuesque poem built on the model of antiquity, and challenging its model. And *Hermann and Dorothea*, a somewhat Virgilian picture of our European countryside, told in faultlessly rhythmic verse, but again with its rural content and virtuous thrift and wedded life and quiet courage settled along the very fringe of war. It had its imitators; one was, I imagine, Longfellow's *Evangeline*, a late echo from across the Atlantic. It also influenced Clough, and not only in metre. Then there are the *Wilhelm Meister*, and *Wilhelm Meister's Travels*, and the *Journey to Switzerland*, and the *West-Oestlicher Divan*, and the dramas of *Goetz von Berlichingen*, *Egmont*, and *The Natural Daughter*. For 18 years he was the Director of the Grand Ducal theatre at Weimar, and the Grand Duke gave him a free hand to manage it as seemed best to him, within a certain expenditure. This management was a lively interest to him, and he faintly regretted in old age that he had spent so much time on it. A playwright's question at that time in Germany was adherence to the classical unities of time and scene. Goethe in some plays departed fully from them, in others not. His *Poetry and Truth* is autobiography of his youth and early middle age. The *Conversations* by Eckermann continues that theme to his death. It is often compared with Boswell's *Life of Johnson*, but this latter is too much the superior to make the comparison instructive. Eckermann was painstaking, but a "slow person." Goethe did not open his heart to him intimately; he treated him somewhat as a retainer. Goethe was a man who customarily in his study wore his "star"—his Court decoration. Eckermann's wife was never on Goethe's reception list, although he showed personal kindness to Eckermann. Goethe gloried in the Court functions of Saxe-Weimar. He was never an admirer of the French Revolution. He admired Canning's support of Portugal. He praised the freedom of the English way of life, but thoroughgoing egalitarianism scared him. I should suppose him, translated into English terms, a moderate conservative. In religion he was essentially a theist, although at the latter end of his life he protested against not being regarded as a Christian. He condemned such expressions as "the Lord God" and "good God" applied to an "incomprehensible Being beyond the reach of our thoughts." He felt that to address prayer to such a Being was unseemly. As to human personal immortality he was in doubt; about such questions it was the part of a wise man who had work to do to do it and not puzzle himself with the questions.

But I fear I am neglecting part of what was asked of me—namely, Goethe's scientific writings. To appraise them is not a congenial task. In his time natural science was commonly called natural philosophy or simply philosophy. He busied himself with this off and on throughout his life. He may be called an amateur in it without belittling his position in it. His interest in it was wide, and included zoology and botany as well as geology and physics.

Let us turn to the two first of these and recall where they stood in Goethe's period, say from 1780 to 1832, the date of his death. The microscope was in use, though not so much as the hand lens. Simple visual magnification had, although it did not foresee it, a great generalization awaiting it. The hand lens was not powerful enough for it, but the compound microscope was. It would be able to show, in 1839, that each animal and plant which we see with the unaided eye is a society of living units cohering as a composite individual, the whole shaped into a fish, or bird, or man, or flowering plant, as the case might be. The establishing of this immense fact spelt ruin to much gratuitous theory. To such theorizing Goethe had contributed with enthusiasm. There was a sect of so-called "Philosophers of Nature" who especially cultivated this field. The anatomist Oken taught that skull is a set of fused vertebrae; Goethe went further and declared that primordial vertebra is the basis of structure of the whole tribe of backboned animals. Analogously he taught that in the plants a basic element of structure which pervades them all is an "ideal" leaf. The plant is an assemblage of such modified leaves. These assumptions stood throughout Goethe's life as untested possibilities, but when, soon after his death, the cell-theory and embryology came into being, new criteria became available. Embryology did not reveal elemental vertebrae within the fabric of the skull, nor did the plant resolve itself into primordial leaves. Goethe's guesses then receded into the limbo of untenable hypotheses. But these guesses did serve to chasten the frozen view of species favoured by the Linnean classification and to substitute for it an idea of fluctuation of a specific form about a mean. Goethe attributed this fluctuation to the fancy-free operation of a creative deity which he addressed as Nature, an Olympian being. We have to bear in mind that Goethe was both a poet and a pagan. It was only at the end of his life that, perhaps for appearances, he made some approaches towards the Christian faith—and in doing that he equated Christ and the sun.

But to return to his science. He propounded yet another "law of Nature." It explained the long body of the snake as being obtained by suppression of the creature's limbs; and the relatively large limbs of the frog by shortening of the creature's body. "Nature" could not add to the animal except at the price of taking something away. But knowledge does not confirm this.

He also turned to the subject of colour. He was what psychology styles "a visual"; that is to say, visual images rather than auditory dominated in his mind. Comparing the eye with the ear, he speaks of the latter as a "dull sense," showing how different is the ear for music from the literary ear. There is a field of colour which centres on "subjective colour"—that is, colour sensible even in absence of physical stimulation. Goethe made a number of excellent observations on this. He also made physical experiments on colour. Professor Andrade, the accomplished physicist and also historian of science, comments in the current issue of *Nature* on Goethe's pronouncements in this field and there is no need for me, who am far less competent, to dilate upon them here. Suffice it to say that Goethe rejected the fundamental observation on white light and the prism. He reverted to a modification of the Aristotelian theory of classical antiquity. In his great *Handbuch*, first issued in 1856, Helmholtz dismissed Goethe's view as not based on science at all.

Goethe was a man who greatly impressed his contemporaries. His self-confidence as a scientific theorist was that of an enthusiast and amateur. He said, and repeated, "I do not attach importance to my work as a poet, but I do claim to be alone in my time in apprehension of the truth about colour." Here a great artist was mistaken in appraising his own gifts. We learn how necessary in the make-up of science is, along with the urge to discovery, the sublime detachment of the true scientific thinkers.

---

The report of the final conference of the British Hospitals Contributory Schemes Association, which was held at Folkestone on Sept. 30–Oct. 3, 1948, has been published. A limited number of copies are available on application to the honorary secretary of the association at Royal London House, Queen Charlotte Street, Bristol, 1.

# STREPTOMYCIN TREATMENT OF SEPTICAEMIA AND MENINGITIS DUE TO INTESTINAL ORGANISMS IN INFANTS

BY

ROBERT DEBRÉ

AND

PIERRE MOZZICONACCI

With the Collaboration of RAYMONDE GRUMBACH, PIERRE BOULARD, LUCIEN COSTIL, and JANINE MEYER

*From the Faculty of Medicine, University of Paris*

The effectiveness of streptomycin on Gram-negative organisms of the *Bact. coli* and *Salmonella* groups *in vitro* was quickly recognized by Waksman and others, and has led clinicians to make use of this property in the treatment of infection by intestinal organisms. Since 1945 encouraging results of the use of streptomyin have been reported in urinary infections (Helmolz, 1945) and miscellaneous conditions (Herrel and Nichols, 1945). Several authors have confirmed these results (Keefer *et al.*, 1946; Goettsch *et al.*, 1948), and we ourselves, struck with the frequency of septicaemia and meningitis of this type in the newborn and the infant, have reported our preliminary investigations (Debré, Mozziconacci, Grumbach, and Boulard, 1948).

We were able to collect 41 cases of infection due to organisms of the *Salmonella* groups and of the *Bact. coli* and similar groups—infection which previously was fatal but in which streptomycin has given appreciable results. We think, however, that our technique might be improved and we hope for still better results in the future.

The 41 cases include all infections, slight or severe, during the course of which bacteriaemia was demonstrated either by blood culture or by the development of metastatic abscesses, or both. We have not included mild infections of the urinary tract in this series.

## Clinical Picture

The clinical picture, no matter what the organism, presents the same general features. At the onset the infection may be subacute, with failure to gain weight (23 cases), or with diarrhoea and vomiting (sometimes severe) that often ceases after a few days. There may be a persistent irregular fever of about 38–39° C., anorexia, and progressive loss of weight. The stools may indicate faulty digestion. In 11 of our patients these features continued during the entire illness; in eight others a neurotoxic state was superimposed. In other cases the infants rapidly became dehydrated and critically ill. The onset may also be marked by signs suggesting acute meningitis (8 cases). In our series, cases with meningitis due to Friedländer's bacillus were the only ones giving rise to clear-cut signs of the condition. Cases complicated by meningitis should be considered separately, owing to their more grave prognosis. We have therefore divided our series into (*a*) 16 cases of septicaemia without meningitis, and (*b*) 25 cases of meningitis with or without septicaemia.

Alimentary symptoms dominate the clinical picture in the septicaemic forms of the disease. Diarrhoea occurred in 29 cases out of the 41. The stools often had a peculiar odour and were sometimes orange-coloured. Vomiting occurred in 30 cases, and in 16 of these it ushered in the disease. In four cases the stools contained fresh blood and mucus, as in the dysenteric colitis of older children. Abdominal distension was a striking feature. In several cases oedema of the abdominal wall was present, particularly in the subumbilical region, and sometimes oedema of the genitalia as well. In one case there was a red periumbilical swelling. Purpura often occurred on the abdominal or thoracic walls. Usually no splenomegaly was present, but the liver was sometimes enlarged. In four cases there was hepatomegaly alone and in three cases jaundice, which was accompanied in two patients by abdominal distension and the appearance of a collateral circulation. In some cases there were areas of localized gangrene.

The temperature was always raised, often to 38–39° C.; sometimes it reached 40° C. Loss of weight accompanied the infection, and often a rapid loss preceded the rise in temperature by 24 to 48 hours. There were also loss of appetite, intense dehydration, and frequently cyanosis, even without pulmonary signs. Localized suppuration, for which systematic search should be made, may occur as otitis, pyelitis, or meningitis. Otitis and mastoiditis were found in 18 cases, and many authors have considered this route to be the means by which the meninges are infected. The organism obtained from blood culture is not invariably that recovered from the middle ear. Pyuria was found in 16 cases, in almost all of which the infective organism was *Bact. coli.* In every case the organisms in the urine were the same as those recovered from the blood and the meninges. Infection was, however, most often localized in the meninges, and it is necessary not only to search carefully for physical signs but to perform lumbar puncture in all cases.

It has recently been shown that in infections by intestinal organisms there is a raised white cell count in which polymorphs predominate (Debré, Grumbach, and Mozziconacci, 1948). All our cases except four had a leucocytosis of over 10,000 per c.mm., the count occasionally reaching 63,000–83,000. The average number of polymorphs was 72%; as the red blood count was not altered the condition was obviously a pure leucocytosis, and did not represent haemoconcentration or the marrow reaction of the acute infectious anaemias of infancy. Infections with *Pseudomonas pyocyanea* sometimes produce exceptions to this rule.

Blood cultures were positive in 27 cases out of 32. In many cases culture was performed aerobically and anaerobically. The organisms grew rapidly in a simple aerobic medium, and the only difficulty was their exact identification. Treatment with streptomycin should be started once a Gram-negative organism has been isolated. Without doubt final success depends on early treatment, and non-meningitic forms so treated are likely to be cured (12 cases out of 16 in our series).

Recovery is usually rapid. The alimentary disturbances disappear first, the temperature falls to normal, and there is a gain in weight. A relapse may occur, and there is always the risk that the second attack will involve the meninges. In fatal forms of the disease fatty degeneration of the liver or a subclinical meningitis may be discovered at necropsy.

Meningitic forms of the disease are the most serious and the most difficult to treat. Out of the 41 cases we had 25 cases of meningitis, of which only four have been definitely cured. In many instances the dominant feature of the meningitis was its extreme latency. In 12 out of 25 cases the condition was discovered by lumbar puncture, which was performed after either a positive blood culture or the appearance of slight signs suggesting meningeal irritation. In 13 cases, however, the meningitis was revealed

by the classical signs. In some cases it resembled pneumococcal meningitis. The cerebrospinal fluid was usually frankly purulent and the organism could be recovered from it. But the fluid may be clear, with only a lymphocytic reaction and a raised albumin to suggest the possibility of meningitis. In three cases the cerebrospinal fluid was normal in all respects, although severe suppurative meningitis was revealed at necropsy. Of the 25 cases only four were cured, and four became chronic.

Cure seems to be possible only in cases that are treated promptly: two who were eventually cured were treated when the cerebrospinal fluid was still clear and showed only an increase in lymphocytes and albumin. If treatment is insufficient or too late the patient may die or the disease may become chronic and hydrocephalus may appear. One of our patients, on whom we had decided to operate, developed hydrocephalus. A ventricular puncture revealed at first a clear fluid, which became opaque at the end of the aspiration and was found to contain *Bact. coli*. These findings precluded further intervention. These cases of hydrocephalus are rapidly progressive and call for operative treatment, but we have not yet seen a case in which this has been successful.

TABLE I.—*Treatment of Septicaemia without Meningitis*

| Case No. | Age | Organism | Previous Illness | Sensitivity *in vitro* | Treatment (Units of Streptomycin) | Clinical Progress | Result | Necropsy Findings |
|---|---|---|---|---|---|---|---|---|
| 1 | 5 months | Bact. coli | — | — | 300,000 I.M. | Slow improvement | Recovered | |
| 2 | 7½ ,, | ,, ,, | — | — | 600,000 I.M. and sulphonamides | Rapid improvement | ,, | |
| 9 | 8 ,, | ,, ,, | — | Blood, 2,000 γ | 300,000 I.M. and sulphonamides | ,, ,, | ,, | |
| 11 | 1 year | Str. pneumoniae | — | — | 1,000,000, later 500,000 I.M. | Improvement then rapid deterioration | Died | |
| 12 | 2 months | Bact. coli | — | — | 600,000 I.M. | Rapid improvement | Recovered | |
| 15 | 2 ,, | ,, ,, | — | Blood, <5 γ | 250,000 I.M.; 100,000 orally; sulphonamides | Progressive deterioration | Died | Fatty degeneration of liver; no meningitis |
| 20 | 1 year | ,, ,, | — | Blood, 1,000 γ | 700,000 I.M.; 100,000 orally | Rapid improvement | Recovered | |
| 25 | 6 months | S. typhi-murium | — | Blood, 30 γ | 400,000 I.M.; 100,000 orally; sulphonamides | Two successive attacks | ,, | |
| 26 | 3 ,, | S. enteritidis | — | Blood, 40 γ | 400,000 I.M. and sulphonamides | Favourable | ,, | |
| 27 | 3 ,, | Bact. coli | — | Blood, 2,000 γ | 600,000 I.M.; 300,000 orally; sulphonamides | Slow, with relapses | ,, | |
| 31 | 1 month | Ps. pyocyanea | — | — | 300,000 I.M. | Very rapid improvement | ,, | |
| 33 | 2½ months | ,, ,, | — | — | — | Rapid deterioration | Died | |
| 34 | 2 ,, | Bact. coli | — | — | 400,000 I.M.; 200,000 orally; sulphonamides | Slow; favourable | Recovered | |
| 35 | 2½ ,, | Str. faecalis | — | Blood, 2,000 γ | 600,000 I.M.; 200,000 orally; sulphonamides | Slow improvement | ,, | |
| 40 | 4 ,, | Bact. coli | — | Pus from ear, 20 γ; Blood, 40 γ | 400,000 I.M. and sulphonamides | Rapid deterioration, then slow improvement | ,, | |
| 41 | 3 ,, | ,, ,, | Congenital syphilis | — | 300,000 I.M. and 200,000 orally | Slow deterioration | Died | |

I.M. = Intramuscular.

## Treatment

Our experience is too limited to allow us to lay down definite rules for treatment. We can only indicate the measures that we have adopted.

*General Infections.*—From 0.05 to 0.1 g. (50,000 to 100,000 units) of streptomycin sulphate or hydrochloride per kg. body weight was given daily. For oral administration 0.1 to 0.3 g. (100,000 to 300,000 units) of streptomycin dissolved in 60 ml. of sugared water was divided into six doses of 10 ml. and given four-hourly. Medication by this route, which had previously given good results (Goettsch *et al.*, 1948), seemed efficacious in treating simple intestinal infections in small children, and therefore appeared to be indicated as an adjuvant in septicaemia. The results are shown in Table I.

*Meningeal Infection.*—This was treated by the intrathecal injection of 0.025 g. of streptomycin dissolved in 5 ml. of warm physiological serum. The injection was made twice in 24 hours for the first five days and once in 24 hours on the following days. When necessary a ventricular injection of 0.01 g. of streptomycin, similarly diluted, was given. This route is not without danger, and we have seen convulsions produced by its use. It should be employed only in cases of ventricular infection not affected by the subdural injection of streptomycin, or in cases of subdural obstruction. The dose injected must be small and well diluted; the injection must be made slowly and an equivalent amount of cerebrospinal fluid removed first. The results are shown in Table II.

We have used sulphonamides with streptomycin, and have favoured sulphadiazine in a dose of 0.3 to 0.4 g. per kg., given by the oral route.

Penicillin was given in cases of superadded infection. These cases of meningitis of mixed aetiology are not exceptional. Neurosurgical treatment is the only measure possible in chronic cases of meningitis with hydrocephalus. Lumbar puncture may be discontinued when the cerebrospinal fluid is sterile—usually after five to eight days. Treatment with intramuscular streptomycin should be continued for two to three weeks for fear of relapse.

## Sensitivity of Organisms

The response of the organisms to streptomycin was assayed from time to time during treatment. The method used consisted in inoculating a series of tubes containing the same volume of peptonized water with an equal quantity of organisms, then adding to each of these tubes a progressively increasing amount of streptomycin. After 24 hours note was taken of the dilutions in which turbidity was absent. We have made similar studies with solid media, which is a more precise method and allows the colonies to be counted.

The sensitivity of organisms so far studied has often been considerable—of the order of 3 to 7 γ per ml.: that is, it required 3 to 7 units of streptomycin to inhibit growth in 1 ml. of the culture. We could expect treatment to be effective in the case of organisms sensitive to 20 to 30 γ per ml. But this method estimates only bacteriostasis and not bacteriolysis, which is an important cause of error and explains certain discrepancies between sensi-

TABLE II.—*Treatment of Meningitis with or without Septicaemia*

| Case No. | Age | Organism | State on Admission | Delay in Treatment | Sensitivity *in vitro* | Treatment (Units of Streptomycin) | Bacteriological Progress | Clinical Progress | Result | Necropsy Findings |
|---|---|---|---|---|---|---|---|---|---|---|
| 3 | 18 days | Proteus vulgaris | – – – | 3 days | C.S.F. <5 γ | 500,000 I.M.<br>100,000 I.V. | Good | Hyperpyrexia; convulsions | Died | Suppurative arachnoiditis |
| 4 | 8 months | Str. pneumoniae | – – | 1 month (relapse after sulph.) | | 300,000 I.M.<br>100,000 I.V.<br>50,000 I.T. | ,, | Bad | Hydrocephalus; died | |
| 5 | 1 year | ,, ,, | – | 0 | | 900,000 I.M.<br>50,000 I.T.<br>4,000 I.V. sulphadiazine | Improvement then relapse | Improvement then deterioration | Died | |
| 6 | 10 days | Str. pneumoniae, Proteus vulgaris | – – – | 4 days | C.S.F. 20 γ | 300,000 I.M.<br>100,000 I.V.<br>50,000 I.T. | Good | Bad | ,, | Ventricular collapse; pus in two ventricles |
| 7 | 1 month | Str. pneumoniae | – – | 1 month | C.S.F. 3–5 γ | 300,000 I.M.<br>100,000 I.V.<br>50,000 I.T. | ,, | Bad; pneumococcal superinfection | Hydrocephalus; died | Purulent arachnoiditis |
| 8 | 6 weeks | N. meningitidis, Bact. coli | – – | 0 | C.S.F. 4 γ | 800,000 I.M.<br>100,000 I.V.<br>100,000 I.T. | Rapid | Improvement then deterioration | Died | ,, ,, |
| 10 | 1 month | Str. pneumoniae, Bact. coli | – – – | 5 days | Blood 1 γ<br>C.S.F. 30 γ<br>urine 50 γ | 450,000 I.M.<br>50,000 I.T. | Rapid improvement then relapse | ,, ,, | ,, | |
| 13 | 6 months | Bact. coli | – – – | 0 | Blood <5 γ<br>stools and urine >2,000 γ | 500,000 I.M., sulphonamides | Rapid | Bad | ,, | Meningitis found |
| 14 | 10 days | Proteus vulgaris | – | 10 days | | 200,000 I.M.<br>30,000 I.T., sulphonamides | | Improvement then rapid deterioration | ,, | |
| 16 | 2 months | Bact. coli | – – | 0 | C.S.F. >2,000 γ<br>blood 5 γ<br>urine >2,000 γ | 300,000 I.M.<br>30,000 I.T. | ,, | Slow improvement | Recovered | |
| 17 | 17 days | Bact. coli, Str. pneumoniae | – – – | 6 days | | 600,000 I.M.; penicillin<br>600,000 I.M.,<br>25,000 I.T. | No improvement | Rapid deterioration | Died | Pus at base of skull |
| 18 | 19 ,, | Str. faecalis | – – | 0 | Blood 100 γ | 200,000 I.M.<br>50,000 I.T. | Nil | Bad | ,, | |
| 19 | 27 ,, | Bact. coli | – – – | 2 days | | 300,000 I.M. | | ,, | ,, | Meningitis found |
| 21 | 7 weeks | ,, ,, | – – – | 4 ,, | | 150,000 I.M. | | Progressive deterioration | ,, | ,, ,, |
| 22 | 17 days | S. typhi-murium | – | 8 ,, | C.S.F. 80 γ | 200,000 I.M.<br>50,000 I.T. | Nil | Bad | ,, | |
| 23 | 5 months | Ps. pyocyanea | – – – | 15 ,, | C.S.F. 40 γ | 1,000,000 I.M.<br>100,000 I.V.<br>50,000 I.T. | Rapid | ,, | ,, | Purulent arachnoiditis |
| 24 | 1 month | Bact. coli | – | 1½ months | C.S.F. <50 γ<br>stools 500 γ | 300,000 I.M.<br>25,000 I.T., sulphonamides | ,, | Relapse, then deterioration | Hydrocephalus; died | |
| 28 | 4 months | Str. pneumoniae | – – – | 0 | C.S.F. 7 γ | 500,000 I.M.<br>25,000 I.T.<br>100,000 orally | Good | Toxic relapse | Recovered | |
| 29 | 2 ,, | Bact. coli | – | 15 days | | 400,000 I.M.<br>12,000 I.T.<br>12,000 I.V. | Rapid in C.S.F., slow in ventricular fluid | Cachexia; hydrocephalus | Died | Hydrocephalus; suppurative ependymitis of 4th ventricle |
| 30 | 3 ,, | Ps. pyocyanea | – – – | 15 ,, | C.S.F. 3 γ | 800,000 I.M.<br>25,000 I.T., sulphonamides | Rapid, then reappearance of organisms | Improvement, then relapse | ,, | |
| 32 | 27 days | ,, ,, | – – – | 4 ,, | | 400,000 I.M.<br>15,000 I.T. | | Rapid deterioration | ,, | |
| 36 | 1½ months | Bact. coli | – – – | 0 | | 300,000 I.M.<br>15,000 I.T.<br>100,000 orally, sulphonamides | Rapid | Rapid improvement, then relapse | Recovered | |
| 37 | 1 month | Salmonella | – – – | 5 days | C.S.F. 150 γ | 400,000 I.M.<br>25,000 I.T.<br>25,000 I.V. | Nil | Rapid deterioration | Died | Pus on vault, base, and spinal cord |
| 38 | 15 months | Ps. pyocyanea | – | 0 | C.S.F. 2,000 γ | 800,000 I.M.<br>200,000 orally<br>25,000 I.T.<br>sulphonamides | Rapid | ,, ,, | Recovered | |
| 39 | 4½ ,, | Bact. coli | – | 6 days | Blood 50 γ<br>urine 2,000 γ | 500,000 I.M.<br>200,000 orally<br>20,000 I.T.<br>sulphonamides | | Progressive deterioration | Died | Brain congested; thin fibrinous film at the base |

I.M. = Intramuscular. I.V. = Intraventricular. I.T. = Intrathecal.

tivity of the organism *in vitro* and the clinical progress of the disease. We have proved this by centrifuging in five cases the clear (and therefore apparently sterile) tubes and culturing the deposit on agar. Although the five cultures originally appeared to be sensitive to concentrations of streptomycin of 1 γ, 10 γ, 20 γ, 40 γ, and 200 γ, respectively, it was demonstrated that the newly cultured organisms were still living and could grow in media containing 10 γ, 50 γ, 20 γ, and 500 γ of streptomycin. The organisms had therefore not been destroyed, but their development had been inhibited. The sensitivity of the organisms varied greatly from case to case, according to whether they were recovered from the urine, the blood, or the cerebrospinal fluid. The sensitivity of those affecting the meninges is obviously the most important.

It was not possible to estimate the resistance of the organisms in all our cases, but our results show that there is no clear relation between the resistance of the organisms and the clinical progress of the case. The progress of the patient is determined not only by his response to streptomycin but also by anatomical lesions and the obstruction they present to the diffusion of antibiotics. This is, in our opinion, the reason for the difference between the relatively favourable prognosis in cases with septicaemia and the extreme gravity of those with meningitis. All the necropsies on cases of meningeal infection have shown a purulent arachnoiditis at the base of the skull which was almost always associated with marked ventricular distension whether there was clinical hydrocephalus or not. It does not seem to us that these lesions acted by the simple

mechanism of producing ventricular block, but it is certain that they affected the circulation of the cerebrospinal fluid and the diffusion of streptomycin injected subthecally.

### Comment

We cannot close this paper without remarking on the relative frequency of infection by intestinal organisms in infants. In many circumstances saprophytic organisms in the digestive tract of the newborn become pathogenic and produce bacteriaemia, septicaemia, and meningitis. It is significant that in 18 months we have been able to observe in the Clinique Médicale des Enfants 41 cases of this type of infection, 25 of which developed meningitis. The signs of these infections are often obscure at first sight, and many of the cases can be discovered only by the careful examination of infants suffering from toxaemia and subacute fever with alimentary disturbances.

A search must be made for the organism in blood, marrow, stools, urine, pus from the ear, cerebrospinal fluid, nasopharyngeal secretions, and pus from any metastatic suppuration in the skin. Repeated blood culture is extremely important. The occurrence during a gastro-intestinal illness of an inexplicable alteration in the patient's general condition or, as we have shown, a polymorphonuclear leucocytosis, is a diagnostic sign of great importance. The possibility of meningeal infection must always be considered, and lumbar puncture, repeated if necessary, must be done as a routine measure. At the same time it must be remembered that the cerebrospinal fluid may be normal or be little changed.

### Summary

An account is given of 41 cases of infection in the infant by intestinal organisms, seen over a period of 18 months. Of these cases 16 had septicaemia alone and 25 developed meningitis.

The clinical features of the condition are discussed, and an account is given of treatment with streptomycin given by the intramuscular, oral, intrathecal, and intraventricular routes.

A method of assaying the sensitivity of organisms to streptomycin *in vitro* is discussed.

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The family allowances scheme has now been in operation for three years. The Ministry of National Insurance states that about 2,941,000 families of two or more children are receiving allowances varying between 5s. and £3 5s. a week at a total cost of £60 million a year. Family allowances are a payment of 5s. a week for every child after the elder or eldest below the age limit, which is usually 15 (school-leaving age), but is extended to July 31 following the sixteenth birthday where full-time education is continued and in cases of apprenticeship. During the three years the Ministry has received nearly three and a half million claims to family allowances, of which fewer than 100,000 have had to be rejected. The 2,941,000 families receiving allowances contain children within the qualifying ages as follows: two children, 1,850,000; three children, 688,000; four children, 247,000; five or more children, 156,000. The family drawing the largest allowance of £3 5s. a week consists of 14 children within the age limits. In the last year over 290,000 new claims to allowances resulted in payments for over 300,000 children. In the same period the total number of allowances in payment and the number of children for whom allowances are paid increased in each case by over 100,000.

# STREPTOMYCIN TREATMENT OF INFANTILE DIARRHOEA AND VOMITING

BY

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Crowley *et al.* (1941), in a survey of the literature and from their own findings, concluded that no single specific aetiological agent could be incriminated in infantile diarrhoea and vomiting. A wealth of facts relating to the clinical and metabolic changes arising in that condition has been accumulated and has made treatment more rational and effective; none the less, modern medical science has not yet provided the answer to the challenge of this illness. It is therefore not surprising that almost every chemotherapeutic agent introduced during the last decade has been tried in the treatment of infantile diarrhoea and vomiting in the vain hope that it might offer a satisfactory solution to the problem.

Recently streptomycin has been used and a number of encouraging results have been published. James, Kramer, and Armitage (1948) treated 30 children aged from 6 days to 13 months with streptomycin by mouth, on the basis of their finding in the stools *Proteus vulgaris*, to which they attributed pathogenic significance. They pointed out that some of their cases not associated with *Pr. vulgaris* also improved on streptomycin. There were no deaths in their series, and convalescence was particularly rapid. In a control group of eight cases *Pr. vulgaris* was isolated from the stools of five infants; all recovered, though at a slower rate. The total dose of streptomycin was 2 g., given over a period of seven days. No toxic effects were noticed, and *Pr. vulgaris* was rapidly cleared from the gut as a result of treatment.

Pulaski and Amspacher (1947) reported an epidemic involving 13 infants, three of whom died; the successful outcome in the ten who recovered was attributed directly to streptomycin. The dosage used in all the cases was 0.1–0.2 g. of streptomycin per kilogram of body weight by mouth for two to ten days. Loeschke and Cochlovius (1949) attributed recovery from infantile gastro-enteritis to streptomycin in 9 of 13 cases. They gave 25–75 mg. five to eight times daily by mouth. Their bacteriological findings were *Bact. coli*, *Pr. vulgaris*, *Pseudomonas pyocyanea*, and *Streptococcus faecalis*. A reduction in the number of Gram-negative organisms isolated generally followed the oral administration of streptomycin. Leisti (1947) recorded his results in 46 infants suffering from diarrhoea; 38 were full-term babies, eight of whom died; 8 were premature infants, all of whom recovered. Streptomycin was given in a dosage of from 40,000 units (40 mg.) to 160,000 units (160 mg.) intramuscularly daily for one to eight days. Goettsch, Cobley, and Mulloy (1948) obtained excellent results in 44 cases of parenteral gastro-enteritis. There were three deaths in their group, which they felt could not be attributed to failure of streptomycin. Their dosage was 0.5 g. intramuscularly and 0.5 g. orally for seven to ten days.

In the present investigation special attention was given to the presence in the stools of a serological type of *Bact. coli* var. *neapolitanum* (abbreviated in this paper to B.C.N.) and *Pr. vulgaris*, the object being to correlate the clinical effects of treatment with bacteriological findings. Organisms of the *Salmonella* and *Shigella* groups were absent in this series of cases. Bray (1945), Bray and Beavan (1948), Giles and Sangster (1948), and Taylor, Powell, and Wright (1949) have all described this particular serological type of *Bact. coli* associated with a high percentage of cases of infantile diarrhoea and vomiting. Dr. C. Giles kindly placed at the disposal of one of us (G.M.) antisera and subcultures of his alpha and beta types of *Bact. coli*, from which our own antisera were prepared (the alpha type corresponding to B.C.N.). Full details of the bacteriological investigations and findings will be published later.

Stools were cultured before streptomycin was given and just before or after the end of treatment. No case was considered to be negative for B.C.N. until at least 30 colonies had been tested specially. The streptomycin sensitivity of B.C.N. strains was tested on plates, using strips of filter-paper soaked with 1 mg. per ml. of streptomycin.

## Results of Treatment

Cases of non-specific infantile diarrhoea and vomiting admitted to hospital, as well as those developing the disease after admission, were divided into three groups. One group was treated with streptomycin by intramuscular injection, a second group by oral administration, while every third case, regardless of its severity, acted as a control and formed the third group.

Two standard schemes of dosage were employed for both the intramuscular and the oral route of administration. The first was to give 20 mg. of streptomycin per lb. body weight per day, divided into doses given at four-hourly intervals day and night for five to seven days; the second was to administer 100 mg. at four-hourly intervals for 24 hours and 75 mg. at four-hourly intervals for the remainder of the period, which varied from four to six days. The total dosage used for a single case therefore rarely exceeded 3 g. Five to seven days' treatment was regarded as adequate for assessment of failure or success.

All patients were given fluids, whether receiving streptomycin or not. The following fluids were used: plasma, blood, 5% glucose in N/5 saline, Hartmann's solution, 2.5% or 5% casydrol intravenously, according to the requirements of the individual infant. Feeding was started after 24 or 48 hours with a diluted skimmed lactic acid milk, gradually increasing the concentration of the formula if improvement was maintained. During the starvation period Hartmann's or Darrow's solution was given by mouth.

The clinical condition of each patient was classified as mild, moderate, or severe, according to the degree of dehydration, character of stools, persistence of vomiting, and initial loss of weight. The existence and the nature of parenteral infection were noted.

The effect of treatment was assessed by the clinical response. Some cases improved rapidly and recovered during the course of streptomycin treatment, and it was these which had to be considered as possibly benefiting from streptomycin therapy. Others showed no improvement during the period when streptomycin was given, but recovered eventually; these were considered not to have responded to streptomycin. Fourteen (19%) of the patients died.

Two levels of dosage have been mentioned, but as there was no apparent benefit from the higher dosage no differentiation has been made in analysing the results.

Table I sets out the number of cases, classed according to clinical severity and the response to treatment. The control group and the cases as a whole are included for comparison.

The details of individual cases are shown in Tables II, III, and IV.

## Bacteriological Observations

Of the 79 cases in this series, B.C.N. was isolated from the faeces at the first examination in 50 (63%). It was more commonly present in severe cases (76%) than in moderate and mild cases (50%). The difference is statistically significant, as it is just over twice the standard error. Of severe cases in which the organism was found, 42% ended fatally (13 of 31 cases). In comparison, of the severe cases which did not have the organism 10% were fatal (1 of 10 cases). This difference is also significant statistically, being more than twice the standard error.

One may therefore conclude that in this series there was a significant correlation between severity of case and the presence of B.C.N., and also between the probability of death in severe cases and the presence of this organism.

TABLE I.—*Details of Cases showing Clinical Severity and Response to Treatment*

| | Intramuscular Treatment | | | | Oral Treatment | | | | Control | | | | Total | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Total Cases | Rapid Improvement | Delayed Improvement | Died | Total Cases | Rapid Improvement | Delayed Improvement | Died | Total Cases | Rapid Improvement | Delayed Improvement | Died | Total Cases | Rapid Improvement | Delayed Improvement | Died |
| Clinical condition of all cases: | | | | | | | | | | | | | | | | |
| Severe .. .. | 16 | 3 | 8 | 5 | 14 | 5 | 3 | 6 | 11 | 8 | — | 3 | 41 | 16 | 11 | 14 |
| Moderate .. | 7 | 6 | 1 | — | 10 | 8 | 2 | — | 14 | 14 | — | — | 31 | 28 | 3 | — |
| Mild .. .. | 1 | 1 | — | — | 2 | 2 | — | — | 4 | 4 | — | — | 7 | 7 | — | — |
| Total .. | 24 | 10 | 9 | 5 | 26 | 15 | 5 | 6 | 29 | 26 | — | 3 | 79 | 51 | 14 | 14 |
| Cases with parenteral infections: | | | | | | | | | | | | | | | | |
| Severe .. .. | 7 | 2 | 3 | 2 | 4 | 2 | — | 2 | 3 | 3 | — | — | 14 | 7 | 3 | 4 |
| Moderate .. | 3 | 3 | — | — | 3 | 3 | — | — | 4 | 4 | — | — | 10 | 10 | — | — |
| Mild .. .. | 1 | 1 | — | — | 1 | 1 | — | — | 2 | 2 | — | — | 4 | 4 | — | — |
| Total .. | 11 | 6 | 3 | 2 | 8 | 6 | — | 2 | 9 | 9 | — | — | 28 | 21 | 3 | 4 |
| Cases without parenteral infections: | | | | | | | | | | | | | | | | |
| Severe .. .. | 9 | 1 | 5 | 3 | 10 | 3 | 3 | 4 | 8 | 5 | — | 3 | 27 | 9 | 8 | 10 |
| Moderate .. | 4 | 3 | 1 | — | 7 | 5 | 2 | — | 10 | 10 | — | — | 21 | 18 | 3 | — |
| Mild .. .. | — | — | — | — | 1 | 1 | — | — | 2 | 2 | — | — | 3 | 3 | — | — |
| Total .. | 13 | 4 | 6 | 3 | 18 | 9 | 5 | 4 | 20 | 17 | — | 3 | 51 | 30 | 11 | 10 |

TABLE II.—*Intramuscular Streptomycin Treatment of Infantile Diarrhoea and Vomiting*

| Case No. | Age | Sex | Clinical Condition | | Bacteriology of Stools | | Result |
|---|---|---|---|---|---|---|---|
| | | | | Parenteral Infection | Before Treatment | After Treatment | |
| 3 | 6 weeks | F | Severe | | B.C.N. (S.) | B.C.N. (S.) | N.I.* |
| 8 | 11 months | M | Moderate | Upper resp. infection | *Pr. vulg.* | *Pr. vulg.* | Improved |
| 9 | 3 weeks | F | ,, | | B.C.N. (R.) | Negative | N.I. |
| 10 | 10 weeks | F | Severe | | *Pr. vulg.* | *Pr. vulg.* | N.I. |
| 11 | 3 ,, | M | ,, | | B.C.N. (R.) | B.C.N. (S.) | Died |
| 12 | 3 ,, | F | ,, | | B.C.N. (S.) | B.C.N. (S.) | Improved |
| 17 | 3 ,, | M | ,, | Otitis media | B.C.N. (S.) | | Died |
| 18 | 10 ,, | F | Mild | Upper resp. infection | *Pr. vulg.* | *Pr. vulg.* | Improved |
| 19 | 3½ months | F | Moderate | | *Bact. coli* (beta) (S.) | Negative | ,, |
| 23 | 4 ,, | F | Severe | | *Pr. vulg.*<br>*Bact. coli* (beta) (S.) | No *Proteus*<br>*Bact. coli* (beta) (R.) | N.I. |
| 26 | 2½ ,, | M | ,, | Otitis media | *Pr. vulg.*<br>*Bact. coli* (beta) (R.) | Negative<br>*Pr. vulg.* | Improved |
| 27 | 5 weeks | M | ,, | ,, ,, | B.C.N. (S.) | B.C.N. (R.) | N.I. |
| 32 | 1 year | F | ,, | ,, ,, | B.C.N. (R.) | | Died |
| 34 | 4 months | F | Moderate | | B.C.N. (R.) | B.C.N. (R.) | Improved |
| 45 | 7 ,, | M | ,, | ,, ,, | B.C.N. (S.) | B.C.N. (R.) | ,, |
| 47 | 3 weeks | M | Severe | | B.C.N. (S.) | B.C.N. (R.) | N.I. |
| 50 | 5 months | F | ,, | Mastoiditis | B.C.N. (S.) | | Improved |
| 54 | 2 ,, | F | Moderate | | B.C.N. (R.) | B.C.N. (R.) | ,, |
| 59 | 4 weeks | F | ,, | Pneumonia | Negative | Negative | ,, |
| 67 | 2 months | M | Severe | | Negative | Negative | N.I. |
| 76 | 5½ ,, | M | ,, | | B.C.N. (S.) | B.C.N. (R.) | Died |
| 77 | 6½ ,, | F | ,, | Pyelitis | B.C.N. (R.) | | N.I. |
| 84 | 2 ,, | M | ,, | | B.C.N. (R.) | | Died |
| 86 | 18 ,, | F | ,, | Otitis media, pyelitis, pink disease | B.C.N. (S.) | B.C.N. (R.) | N.I. |

* N.I. = Not improved, but recovered later on routine treatment. S. = Streptomycin-sensitive. R. = Streptomycin-resistant.

These findings may not, however, apply generally, and in themselves may not indicate a causal relationship.

The organism was often found in mild and moderate cases. It also persisted in recovered cases, even those which had been clinically severe. Of 50 recovered cases it was found in 27 (54%), which was a very small reduction compared with the initial incidence of 63% if a causal relationship existed.

About half the cases from which the organism was isolated before treatment yielded streptomycin-resistant strains (24 of 50 cases, 48%). Strains which were initially sensitive often became resistant during treatment, a change which was noted in 12 of 16 cases (Tables II and III). Five of these 12 cases recovered satisfactorily.

The findings as a whole may be regarded as not supporting an aetiological relationship of this organism to infantile diarrhoea and vomiting. They indicate, too, that streptomycin therapy had little effect in eliminating the organism from the bowel.

*Pr. vulgaris* was isolated initially in 10 cases, in 6 cases being associated with B.C.N. or the beta type of *Bact. coli*. Seven of the 10 cases were classified as severe. This organism appeared to have a minor significance in this series. It was not present in any of the patients who died.

## Discussion

Our investigations confirm the frequent occurrence of a special type of *Bact. coli*, referred to as B.C.N., in the stools of infants suffering from infective gastro-enteritis, though this association was less common in our cases than in the series reported by Bray and Beavan (1948), Giles, Sangster, and Smith (1949), and Taylor, Powell, and Wright (1949). No evidence has yet been forthcoming to prove the pathogenic importance of any of the varieties of *Bact. coli* shown to be associated with infantile diarrhoea.

B.C.N. was isolated from 25 of 32 cases arising after admission to hospital; in all probability these were the result of cross-infection, a conclusion that was supported

TABLE III.—*Oral Streptomycin Treatment of Infantile Diarrhoea and Vomiting*

| Case No. | Age | Sex | Clinical Condition | | Bacteriology of Stools | | Result |
|---|---|---|---|---|---|---|---|
| | | | | Parenteral Infection | Before Treatment | After Treatment | |
| 2 | 2 weeks | F | Severe | | B.C.N. (S.) | B.C.N. (S.) | Died |
| 5 | 5 months | F | Moderate | | Negative | Negative | Improved |
| 13 | 5 ,, | M | Mild | Otitis media | B.C.N. (S.) | B.C.N. (R.) | ,, |
| 15 | 7 weeks | M | Severe | Bronchitis | B.C.N. (R.) | B.C.N. (R.) | N.I.* |
| 28 | 3½ months | F | ,, | | B.C.N. (S.) | B.C.N. (S.) | N.I. |
| 30 | 3 weeks | M | Moderate | Pneumonia | Negative | Negative | Improved |
| 31 | 2 months | F | ,, | | B.C.N. (R.) | B.C.N. (R.) | ,, |
| 40 | 5 ,, | M | Severe | | Negative | Negative | ,, |
| 46 | 6 weeks | M | Moderate | Bilateral otitis media | B.C.N. (S.) | B.C.N. (R.) | ,, |
| 48 | 5 ,, | M | Severe | | Negative | B.C.N. (R.) | N.I. |
| 49 | 3 months | M | ,, | | B.C.N. (R.) | B.C.N. (R.) | Improved |
| 51 | 14 days | M | Moderate | Upper resp. infection | B.C.N. (S.) | B.C.N. (R.) | ,, |
| 53 | 3 weeks | F | Severe | | B.C.N. (R.) | B.C.N. (R.) | Died |
| 55 | 4 ,, | M | Moderate | | Negative | B.C.N. (R.) | N.I. |
| 57 | 3 ,, | F | ,, | | Negative | B.C.N. (R.) | Improved |
| 58 | 9 ,, | M | ,, | | B.C.N. (S.) | B.C.N. (R.) | ,, |
| 60 | 5 ,, | M | Severe | | B.C.N. (R.) | B.C.N. (R.) | ,, |
| 62 | 6 ,, | M | ,, | | B.C.N. (R.) | B.C.N. (R.) | ,, |
| 63 | 3 ,, | M | Moderate | Bronchopneumonia | B.C.N. (R.)<br>*Pr. vulg.* | B.C.N. (R.)<br>No *Proteus* | ,, |
| 64 | 9 months | M | Severe | Bronchitis | B.C.N. (R.) | | Died in 24 hrs. |
| 65 | 3½ ,, | F | ,, | Pneumonia | B.C.N. (R.) | B.C.N. (R.) | Improved |
| 68 | 14 days | M | Mild | | Negative | | ,, |
| 72 | 7 months | F | Severe | Bilateral otitis media | B.C.N. (R.) | | Died |
| 74 | 4 weeks | M | ,, | | B.C.N. (R.) | B.C.N. (R.) | ,, |
| 75 | 11 ,, | M | Moderate | | B.C.N. (S.) | B.C.N. (R.) | N.I. |
| 79 | 6 ,, | M | Severe | | B.C.N. (S.) | B.C.N. (R.) | Died |

*N.I. = Not improved, but recovered later on routine treatment. S. = Streptomycin-sensitive. R. = Streptomycin-resistant.

TABLE IV.—*Control Cases of Infantile Diarrhoea and Vomiting on Routine Treatment*

| Case No. | Age | Sex | Clinical Condition | | Bacteriology of Stools | | Result |
|---|---|---|---|---|---|---|---|
| | | | | Parenteral Infection | Before Treatment | After Treatment | |
| 4 | 1 year | M | Moderate | | *Bact. coli* (beta) (S.) | | Improved |
| 6 | 3½ months | F | ,, | | B.C.N. (S.) | | ,, |
| 7 | 9 ,, | F | ,, | O.R.I. | Negative | B.C.N. (R.) | ,, |
| 14 | 3½ ,, | F | ,, | Otitis media | B.C.N. (S.)<br>*Bact. coli* (beta) (S.) | Negative | ,, |
| 16 | 10 weeks | M | Severe | ,, ,, | Negative<br>*Pr. vulg.* | Negative<br>*Pr. vulg.* | ,, |
| 20 | 15 months | M | Moderate | | Negative | Negative | ,, |
| 22 | 7 weeks | F | ,, | ,, ,, | B.C.N. (R.) | | ,, |
| 25 | 4 months | M | Severe | ,, ,, | B.C.N. (S.) | B.C.N. (S.) | ,, |
| 29 | 1 month | F | ,, | | Negative | | Died |
| 35 | 6 months | F | Moderate | | B.C.N. (S.) | Negative | Improved |
| 37 | 6 ,, | F | ,, | Pyelitis and pneumonia | Negative | ,, | ,, |
| 39 | 2 ,, | M | Mild | | *Bact. coli* (beta) (S.) | | ,, |
| 42 | 5 weeks | M | Moderate | | B.C.N. (S.) | | ,, |
| 43 | 10 ,, | F | ,, | Upper resp. infection | Negative | | ,, |
| 44 | 9 months | F | Mild | Pneumonia | Negative | | ,, |
| 52 | 9 ,, | M | Severe | | B.C.N. (R.) | | Died in 24 hrs. |
| 56 | 3 weeks | F | Mild | | Negative | ,, | Improved |
| 61 | 4 months | F | Moderate | | B.C.N. (S.) | ,, | ,, |
| 66 | 10 ,, | M | Severe | | B.C.N. (R.) | ,, | ,, |
| 69 | 7 ,, | F | Mild | Bronchopneumonia | Negative | ,, | ,, |
| 70 | 8 ,, | M | Severe | | B.C.N. (S.) | | ,, |
| 71 | 5 ,, | M | ,, | Upper resp. infection | *Bact. coli* (beta) (S.)<br>*Pr. vulg.* | | ,, |
| 78 | 8½ ,, | M | Moderate | | B.C.N. (R.) | | ,, |
| 80 | 11 weeks | F | Severe | | B.C.N. (R.) | | Died |
| 81 | 4 months | F | Moderate | | B.C.N. (S.) | | Improved |
| 82 | 4 ,, | M | Severe | | Negative | | ,, |
| 83 | 4 weeks | F | Moderate | | *Bact. coli* (beta) (R.) | ,, | ,, |
| 85 | 2 months | M | Severe | | B.C.N. (S.)<br>*Pr. vulg.* | Not received | ,, |
| 87 | 3 weeks | M | ,, | | B.C.N. (R.) | B.C.N. (R.) | ,, |

S. = Streptomycin-sensitive. R. = Streptomycin-resistant.

by the more frequent isolation of streptomycin-resistant strains later in the investigation. This may be accounted for by survival of resistant strains only in patients under treatment or by cross-infection with a B.C.N. strain originally sensitive but resistant after treatment.

Bacteriological investigation thus would not seem to justify streptomycin therapy, though the presence of B.C.N. in a severe case of infantile diarrhoea and vomiting may be regarded as a warning signal and a pointer to a more serious prognosis.

Clinical improvement in some patients receiving the antibiotic seemed to be attained at a more rapid pace than in those treated by standard measures. Especially was this so in cases associated with a parenteral infection: stools returned to normal in a shorter time and the upward trend in the patient's general condition appeared steeper. In agreement with this are the favourable results recorded by Goettsch, Cobley, and Mulloy (1948) in their cases of parenteral gastro-enteritis.

In a number of our cases streptomycin was followed by a spectacular improvement—in others it failed completely. Even detailed analysis of the case histories has not furnished clinical or bacteriological indication for the use of the antibiotic. In each individual case the result of streptomycin therapy was also unpredictable.

## Summary

The results of streptomycin treatment of infantile diarrhoea and vomiting are discussed.

Streptomycin was given to 26 cases orally, and to 24 intramuscularly, while a control group of 29 cases received no antibiotic.

The dosage of streptomycin was either 20 mg. per lb. body weight per day for five to seven days, or 600 mg. for the first 24 hours, followed by 450 mg. daily for a further four to six days.

The results do not indicate that streptomycin exerts any specific therapeutic effect.

The frequent association of a special type of *Bact. coli* (B.C.N.) with infantile diarrhoea and vomiting was confirmed, being found before treatment in 50 out of a total of 79 cases, but no evidence was obtained that it was of any aetiological significance.

Our thanks are due to Professor Gaisford for his encouragement and valuable criticism; to Professor Maitland for allowing facilities in the department of bacteriology and for help with bacteriological problems; and to Drs. S. K. Guthrie, R. I. Mackay, and N. Wells for permission to include some of their cases in our investigation.

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*Food Investigation, 1947*, is a report from the Department of Scientific and Industrial Research (H.M.S.O., price 6d.) which is written for the non-specialist. It describes work which has been done on whalemeat during an expedition to the Antarctic by the factory ship *Balaena*. It was found that the whalemeat was much improved in quality if the whale was bled and cooled down rapidly. The practice recommended was to make an incision in the main blood vessels in the neck and to slit the belly wall so that the cold sea-water could circulate. In this way the meat could be kept in good condition for 18 to 24 hours. Research on meat, fruit, and potatoes continued during the year, and at the Torry Research Station quicker and more convenient methods of freezing were studied. Lobsters are apparently better frozen cooked than raw. Rapidly frozen cooked lobsters can be stored for eight months with little change in flavour and texture.

# THE AETIOLOGY OF GRAVITATIONAL ULCERS OF THE LEG

BY

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The term "gravitational ulcer," first used by Dickson Wright (1931), refers to those chronic ulcers which occur on the lower half of the leg associated with one or more of the following: oedema, cyanosis, induration, sclerosis, pigmentation, loss of hair, eczema, and varicose veins of the affected limb. These are signs of chronic impairment of the venous drainage of the leg. The importance of gravity in the cause of this condition was stressed by Brodie (1846) and by Hilton (1863). Brodie called such ulcers "varicose," and they have long been thought to be due to varicose veins. Gay (1868) was probably the first to show, by clinical observation and careful dissection, that many were due to obstruction of trunk veins, deep and superficial, and that varicose veins often play no part. Gay's work seems to have been forgotten or has been neglected, and the view that varicose veins are the main or only cause has persisted (McPheeters, 1928). Dickson Wright (1931) and Homans (1939) held this opinion, though both believed that some gravitational ulcers were due to thrombosis of deep veins. However, in a series of 432 patients with leg ulcers Birger (1941) found that thrombosis was the chief factor. Nilzén (1945) thought that certainly 41% or possibly 56% of such ulcers were caused by previous thrombosis, Bauer (1946) that 80–90% and Birger (1947) that 40% were due to this cause.

The belief that varicose veins play a major part in the aetiology of these ulcers has affected treatment, which until the last few years has concentrated attention on such superficial varicose veins as might be present.

Allen, Barker, and Hines (1946) considered that chronic venous insufficiency or stasis of the venous blood flow was due to obstruction of one of the main veins of the limb, particularly the ilio-femoral, as the result of thrombophlebitis, neoplastic invasion, or external pressure; incompetency of valves of the ilio-femoral vein resulting from thrombophlebitis without permanent obstruction of the vein; or varicose veins of primary type (i.e., developing spontaneously), particularly those of long standing or considerable extent.

The chief manifestations of chronic venous insufficiency are in the skin and subcutaneous tissue, and are thought to result from venous stasis rather than from increased venous pressure. As a result of stasis the venous blood has a low content of oxygen and a high content of carbon dioxide and other products of metabolism (Dickson Wright, 1931). The nutrition of the tissues is impaired and oedema and necrosis may result. Ulceration of a limb with venous stasis may occur at the site of a local thrombosis of small superficial veins or it may follow trauma with broken skin. The healing power of the poorly nourished tissues is affected and trauma may not be followed by repair. Hence ulceration is a common complication of chronic venous insufficiency. Infection plays little or no part in ulceration (though it may cause thrombosis). There is no relation between the type of infection or the bacteria in the ulcerating area and the slowness or rapidity with which the ulcer heals. Those ulcers which heal most rapidly often contain the most bacteria (Löwenfeld, 1924).

The importance or otherwise of varicose veins in causing chronic venous insufficiency and ulceration is still a matter of dispute. Certain it is that many individuals with severe varices do not suffer from either. Furthermore, patients with chronic venous insufficiency and ulceration of the legs are seen not uncommonly with no varicose veins visible or palpable.

The venous circulation of the limbs can be investigated by clinical examination, including the patient's history, the condition of the limbs, certain special tests (the Brodie–Trendelenburg, Perthes's, etc.), phlebography, venous pressure estimations, examination of veins after surgical removal, and post-mortem dissection.

## Present Investigation

This investigation was undertaken to try to determine the cause of ulceration in a series of 270 unselected patients examined and treated personally. The methods employed were clinical, with phlebography in a few patients.

The term "thrombosis" is used here to denote thrombosis of one of the deep veins of the lower limb, and is assumed to have taken place if there is a history of chronic oedema of the leg of sudden onset, with or without pain and tenderness in the calf and with other signs of persistent venous stasis. Symptoms of pulmonary embolism at the onset and the appearance of varicose veins soon after are taken to indicate that thrombosis occurred.

There were 192 female and 78 male patients. Their ages at the onset of ulceration varied greatly. One woman who had suffered from osteomyelitis of the left leg when aged 3 first developed an ulcer in that leg after slight trauma at the age of 13, and another first developed an ulcer at 17 years while suffering from congenital haemolytic icterus. Ulceration occurred in one youth of 17 a year after a Trendelenburg operation. Most ulcers appeared during the fourth and fifth decades, but in one patient not until the eighth.

*Family History.*—Patients were questioned about the presence of varicose veins or ulceration of the legs in their parents, brothers, sisters, or children. Twelve patients were uncertain and 140 (54%) of the rest gave a positive family history.

*Illustrative Cases.*—Three sisters (unmarried) had gravitational ulcers. Their mother, one of their four brothers, and another sister (married, with five children) had ulcers. Four other sisters were unaffected.

A tram driver had gravitational ulcers. Both his parents had varicose veins and two maternal aunts had ulcers.

Heredity may play a part in the aetiology of ulceration of the legs associated with purpura haemorrhagica, sickle-cell anaemia, congenital haemolytic icterus, splenic anaemia, Gaucher's disease (Witts, 1942), or Cooley's anaemia (Estes, Farber, and Stickney, 1948); otherwise its importance in this condition is not well established. Weber, Rast, and Lutteroti (1930), however, described chronic ulceration of the legs following pneumonia in a man of 25 with thrombo-angiitis obliterans whose father had suffered from similar ulcers, and Carleton (1948) showed a striking family history in two sisters with varicose ulcers. Congenital absence of valves in the veins of the leg as described by Eger and Casper (1943) and Curtis and Helms (1947) may be important in relation to inheritance. Weber (1948) wrote that there certainly is a constitutional tendency to ulcus cruris in some families.

*Occupation.*—Table I shows the occupations followed at the time ulceration appeared. It will be noted that very

TABLE I.—*Occupation*

| Men (Total 78) | | Women (Total 192) | |
|---|---|---|---|
| *Standing* | | *Standing* | |
| Fitter or driller | 10 | Housewife | 132 |
| Labourer | 8 | Shop assistant | 14 |
| Farmer | 5 | Weaver or spinner | 11 |
| Shop assistant | 4 | Office cleaner | 5 |
| Warehouseman | 4 | Canteen worker | 5 |
| Joiner | 3 | Cook or kitchen worker | 5 |
| Gardener | 2 | Hoffman presser | 3 |
| Boiler fireman | 2 | Tailoress (half sitting) | 3 |
| Painter | 2 | Barmaid | 2 |
| Boot repairer | 2 | Landworker | 2 |
| Tailor's cutter | 2 | Hairdresser, laundry hand, varnisher, 1 each | 3 |
| Tailor's presser | 2 | | |
| Baker, bricklayer, circus hand, cleaner, compositor, cook, dentist, engineer, fur cutter, grinder, hairdresser, laboratory attendant, miner, motor mechanic, music-hall artist, optical instrument maker, paper maker, plate-layer, porter, roller coverer, scourer, shoeing smith, steward, tea blender, tram driver, tram conductor, washhouseman, watchman, 1 each | 28 | | |
| Total | 74 | Total | 185 |
| *Sitting* | | *Sitting* | |
| Unspecified | 2 | Unspecified | 3 |
| Clerk | 2 | Office worker | 2 |
| | | Printer | 1 |
| | | Mender | 1 |
| Total | 4 | Total | 7 |

few patients had sedentary jobs, and that many worked standing with little activity as in fitting, drilling, shopkeeping, weaving, and spinning. Although many miners attend this hospital, only one was seen with a gravitational ulcer. Constant muscular effort while working, standing, kneeling, or lying may prevent venous stasis.

*Child-bearing.*—Of the 192 women, 37 (19%) were nulliparous. The remaining 155 had 1 to 15 children each (mean 4.1).

*Weight.*—Obesity has been thought to be of importance in relation to gravitational ulcers (Dickson Wright, 1931; Heller, 1943; Mahorner, 1949). The weight of patients in this series varied between 45 and 132 kg.: a distribution curve is shown in Fig. 1. Nine men and 29 women weighed more than 89 kg., and, of these, four men and twelve women weighed more than 100 kg. One woman weighed 132 kg. It would appear that in the majority of patients with ulcers obesity plays no part in the aetiology.

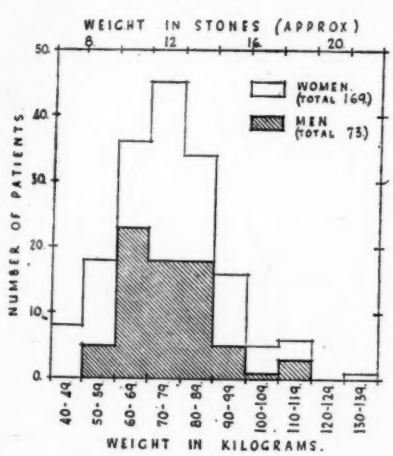


FIG. 1.—Distribution curve of body weight.

*Blood Pressure.*—The blood pressure of 69 men and 172 women was determined. The readings of the women were classified in age groups. The number with systolic pressures above 140 mm. and diastolic pressures above 90 mm. is shown in Table II, with the total in each age group, in order to compare the results with the figures given by Robinson and Brucer (1939) based on a group of 3,405 American urban women taken at random. The proportion of ulcer patients with hypertension is significantly higher than in the control group. The men with ulcers formed a group too small for conclusions to be drawn from their blood-pressure readings.

TABLE II.—*Proportion of Women with Hypertension (172 Patients)*

| Age Group: | 25–9 | 30–4 | 35–9 | 40–4 | 45–9 | 50–4 | 55–9 | 60–4 | 65–9 | 70–4 |
|---|---|---|---|---|---|---|---|---|---|---|
| Total in group | 3 | 4 | 13 | 17 | 20 | 30 | 28 | 32 | 12 | 13 |
| Systolic hypertension: | | | | | | | | | | |
| No. in group | 0 | 1 | 2 | 9 | 9 | 17 | 19 | 28 | 10 | 11 |
| Percentage of group | — | — | 15·3 (5·4) | 52·9 (12·3) | 45·0 (20·9) | 56·6 (21·4) | 67·8 (37·6) | 87·5 (46·5) | 83·3 (57·2) | 84·6 (71·4) |
| Diastolic hypertension: | | | | | | | | | | |
| No. in group | 0 | 1 | 2 | 5 | 5 | 11 | 14 | 21 | 10 | 9 |
| Percentage of group | — | — | 15·3 (5·1) | 29·4 (9·1) | 25·0 (11·5) | 36·6 (10·9) | 50·0 (19·9) | 65·6 (22·5) | 83·2 (26·0) | 69·2 (12·5) |

The figures in parentheses are those of Robinson and Brucer, 1939.

*Concurrent Disease.*—The following diseases were present in addition to ulceration: pernicious anaemia in one patient, severe anaemia secondary to menorrhagia in one, congenital haemolytic icterus in one, diabetes mellitus in four, hyperthyroidism in one, hypothyroidism in one, thrombophlebitis migrans in one, Paget's disease (osteitis deformans) in two, and syphilis in two. The ulceration of the legs of the last two patients had none of the characters of syphilitic ulceration, and antisyphilitic treatment did not cure the ulcers. The Wassermann reaction was also determined in 68 other patients, and was negative. Some of the aetiological factors as disclosed by the history in the present series are shown in Table III.

TABLE III.—*Aetiological Factors in Patients with Gravitational Ulcers*

| | Men | Women | Total |
|---|---|---|---|
| Thrombosis of deep veins: | | | |
| 1. Post-partum thrombosis | — | 69 | 69 |
| 2. Ante-partum thrombosis | — | 15 | 15 |
| 3. Conditions affecting the leg: | | | |
| Injury without fracture | 26 | 34 | 60 |
| Injury with fracture | 6 | 5 | 11 |
| Operation on a leg | 2 | 4 | 6 |
| Infection of the leg | 7 | 8 | 15 |
| Treatment of varicose veins | 8 | 7 | 15 |
| 4. Unknown causes | 8 | 11 | 19 |
| 5. Recumbency or inactivity: | | | |
| Medical illness | 5 | 7 | 12 |
| Operation (not on leg) | 5 | 7 | 12 |
| 6. Miscellaneous causes | 5 | 3 | 8 |
| 7. "Silent" thrombosis (proved) | 0 | 1 | 1 |
| Total | 72 | 171 | 243 (86·6%) |
| Venous stasis with no history of thrombosis: | | | |
| 1. Varicose veins as only cause found | 5 | 24 | 29 |
| 2. Miscellaneous causes | 1 | 1 | 2 |
| Total | 6 | 25 | 31 (11·4%) |
| Grand total | 78 | 196 | 274 |

*Note.*—Four women are entered in more than one group.

## Stasis due to Thrombosis of Deep Veins

### 1. Post-partum "White Leg"

Sixty-nine (36%) women gave a history of post-partum "white leg" (phlegmasia alba dolens)—28 after the first confinement. In the remainder the "white leg" occurred after confinements varying from the second to the thirteenth. Most of the women were multiparae (mean 3.9 confinements), and in six "white leg" occurred after two confinements; in one patient it occurred three times. The mean age at which thrombosis took place was 30.2 years (variation 19 to 46 years). In 27 patients the thrombosis was bilateral and in the others it occurred slightly more commonly on the left side. Only 13 women developed "white leg" after a normal confinement, and one of these got up on the third day, "white leg" developing soon after. Intervention with forceps took place in 18 patients, severe post-partum haemorrhage in 12, a long labour in five, twins in three, abortion at seven months in two, toxaemia of

pregnancy in two, malposition in two, retained placenta in two, ante-partum haemorrhage in one, and triplets in one. Details of other abnormal confinements were not obtained. Matthew (1947) mentioned the raised incidence of "white leg" with high forceps deliveries and stressed the role of infection in some cases. The first ulcers in the present series occurred three months to 27 years after the "white leg" (mean 8.9 years).

*Illustrative Case.*—This patient was delivered of her only child at the age of 25. Details are not available, but she says that it was a difficult labour and forceps were used. A few days later she had "white leg" and "pneumonia" (probably pulmonary embolism). The swelling of the legs persisted, and ten years later, following slight trauma, the first ulcer developed. There was no family history of varicose veins or ulcers of the legs. Her weight was 85 kg. No varicose veins were found on examination, but the legs were oedematous, indurated, and pigmented over the lower halves.

#### 2. Ante-partum Thrombosis

Fifteen patients gave a history of pain and swelling of one or both legs of sudden onset during pregnancy. Oedema of the affected legs persisted and some of the patients developed varicose veins for the first time. It is assumed that thrombosis of the deep veins of the leg had occurred, and in seven patients ulceration of the leg followed within a few weeks. Ante-partum thrombosis is well recognized as a complication of pregnancy, but, as Matthew (1947) pointed out, it is less frequent than post-partum "white leg."

*Illustrative Case.*—A spinner had bilateral varicose veins from the age of 18. Her mother also had varicose veins. At the age of 44, at about the sixth month of her eighth pregnancy, she developed "white leg" (left). She spent the remainder of the pregnancy in bed. An ulcer of the left leg appeared a few months later. She weighed 97 kg. and her blood pressure was 240/110 mm. when she was examined at the age of 52.

#### 3. Conditions Affecting the Leg

*Injury to Leg without Fracture.*—Sixty patients had suffered such an injury to one or both legs. The severity varied from that of a kick to that of a fall from a height, as from a roof or down stairs or through a floor which collapsed (three patients). Other injuries were due to a fall from a tram-car, a superficial gunshot wound of the leg, or wrenching an ankle; many were caused by mild blows such as walking against some firm solid object. In many the skin had not been broken. With most ulcers of the leg the precipitating cause is mild injury with abrasion of the skin. In the group under consideration, patients with a previous history of thrombosis of the leg in whom mild injury produced ulceration are not included. Only those with legs previously normal or with varicose veins with no evidence of chronic venous insufficiency are considered. Of these, 23 gave a history of swelling of the leg after the injury, probably due to thrombosis caused by the injury, and 10 developed varicose veins after the injury, possibly from the same cause. At the time of examination, when ulcers were present, 52 had varicose veins, which in several patients were in the injured leg alone. Slight or moderate injury to the leg with laceration, soft-tissue wounds, or simple haematoma may result in thrombosis. Vance (1934) investigated thrombosis of the veins of the lower extremity and pulmonary embolism as a complication of trauma. He found that even minor injury to the leg may result in thrombosis. Homans (1934), Bauer (1944), Birger (1947), and Mahorner (1949) are in agreement with this view. In Bauer's patients the presence of thrombosis was confirmed by phlebographic examination.

*Illustrative Case.*—A grinder in good health was injured at the age of 32 by a severe blow from an iron girder which fell against his right leg. There was no fracture and the skin was not broken. Swelling of the leg followed. Varicose veins appeared for the first time, and a year later there was ulceration of the affected leg. At the age of 34 the varicose veins were ligated, but the ulceration was not improved. The Wassermann reaction was negative. His father had suffered from ulcers of the leg.

*Injury to the Leg with Fracture.*—This had occurred in 11 patients—affecting the tibia and fibula in six, the femur in two, the patella in one, and the ankle (fracture-dislocation) in two. Both direct injury to a vein and immobilization of the limb may have been factors in causing the thrombosis which followed. Ulceration occurred in a period varying from one month to 26 years (mean 4.8 years) after the fracture.

*Illustrative Case.*—A married woman sustained a fracture-dislocation of the right ankle at the age of 37. The leg was immobilized in plaster-of-Paris for three months, after which it was found to be oedematous and discoloured. These signs persisted, and one month after removal of the plaster ulceration of the leg occurred. There was no family history of ulcers or varicose veins.

*Operation on a Leg.*—Six patients had undergone operation for knock-knee, for hammer-toe, for deformity of the tibia in Paget's disease, for tuberculosis of bone, for osteoarthritis of the hip, and for an unknown cause. In each patient thrombosis of the affected leg had followed the operation, ulceration occurring later.

*Infection of the Leg.*—Fifteen patients had infection of the leg in various forms causing thrombosis: osteomyelitis (2—one of the tibia and one of the patella), septic wounds of the leg (12), and abscess of the ankle drained with tubes (1). One of these patients was a diabetic. Ulceration followed the infection in a period varying from a few weeks to 11 years (mean 4.1 years).

*Illustrative Case.*—A motor mechanic aged 57 caught his left ankle against a sharp piece of metal, an abrasion resulting. This healed, but two weeks later an abscess formed at the site of injury and burst, discharging pus. At the same time the whole leg became swollen, with deep tenderness in the calf. He attended the clinic five months later with an ulcer at the site of the abscess and with oedema and discoloration of the leg. The other leg was normal except for varicose veins, which were prominent in both legs.

*Treatment of Varicose Veins.*—This appeared to be the cause of ulceration in 15 patients, including two in whom the injection of varicose veins was carried out during pregnancy. In two others thrombosis of the leg had occurred previously, in one after a fracture of the patella and in another after a fracture of the humerus which required rest in bed. Injection of varicose veins seemed to intensify the chronic venous insufficiency already present in these patients and to produce it in the remainder. Ulceration of the legs concerned resulted within a few months. The risk of thrombosis of deep veins after the injection of sclerosing fluids into superficial varicose veins, especially above the knee, was stressed by Boyd and Robertson (1947). In three of the patients in the present series varicose veins had been injected at the same time as the internal saphenous vein was ligated, ulceration following within a few weeks. In none had phlebography been carried out to determine the state of the deep venous circulation of the legs before injection of the varicose veins.

*Illustrative Case.*—A married woman suffered from "white leg" (left) after her first confinement at the age of 28, when forceps were used. Varicose veins followed, and these were

injected eleven years later. The left leg became even more oedematous, and ulceration occurred shortly after. Her mother had suffered from varicose veins and ulcers of the leg.

#### 4. Thrombosis of Unknown Cause

Thrombosis in the legs from no apparent cause occurred in 19 patients. In several the condition had started in superficial veins, but all gave a history of marked oedema of the affected leg, with pain in the calf in some, which suggests that the deep veins were involved. Thirteen patients had a family history of varicose veins or ulcers of the legs. Phlebography confirmed the presence of thrombosis (of the femoral vein) in one patient.

*Illustrative Case.*—A nulliparous woman weighing 76 kg. and living an active life suffered from phlebitis of a superficial vein of the left calf for no apparent reason at the age of 36. Within a few days the leg became greatly swollen and pulmonary embolism occurred. Shortly after this the right leg also became swollen. When she was able to walk the oedema increased and ulceration near the left ankle followed. Her mother had suffered from varicose veins and ulcers of the leg.

#### 5. Thrombosis due to Recumbency or Inactivity

*Medical Illness.*—Some illness, the disease itself or the rest in bed necessitated by it, had caused thrombosis of the legs in 12 patients. In three it was said to have been influenza, in two bronchitis (one with pleurisy), and in two lobar pneumonia. Rheumatoid arthritis with many months in bed, pyaemia following a carbuncle, tonsillitis, scarlet fever, and pyrexia of unknown origin were each responsible in the other patients.

*Illustrative Case.*—A baker whose mother had varicose veins developed scarlet fever at the age of 17. Three weeks after the onset, while in bed, thrombosis of the left leg occurred. There were no other complications of scarlet fever. An ulcer of the same leg appeared a few weeks later when he got up. The Wassermann reaction was negative.

*Operations not on the Leg.*—Twelve patients gave a history of "white leg" appearing shortly after an operation. Of these, nine had undergone an abdominal operation—two for appendicectomy (one with drainage), two for removal of ovarian cysts, one for cholecystectomy, one for hysterectomy, one for pelvic abscess, one for abdominal hernia, and one for an operation following an injury, the details of which are not known. Two patients had undergone left inguinal herniotomy and one a perineal operation of unknown type on the bladder for retention of urine. Allen, Barker, and Hines (1946) showed that post-operative thrombosis is more common after pelvic operations than after any other procedure, and more common in the left leg than in the right.

*Illustrative Case.*—A railway plate-layer underwent an operation for left inguinal hernia at the age of 37. Five days later he suffered from pulmonary embolism and shortly afterwards his left leg became swollen. Ulceration of the leg occurred a few weeks after he got up.

#### 6. Thrombosis due to Miscellaneous Causes

Thrombosis of the leg occurred in a woman aged 29 during intravenous therapy with glucose-saline for hyperemesis gravidarum. An ulcer of the ankle followed at the site of injection. The risk of this complication of intravenous therapy when given at the ankle is now recognized.

A woman weighing 117 kg. had varicose veins for years, for which several injections with sclerosing fluids had been given. Thrombosis and ulceration followed a second-degree burn of the right leg. In another woman, aged 59, these followed a scald of the leg.

A miner aged 39, in bed on account of a slight injury to his back, had a thrombosis of the right leg, and ulceration occurred when he got up. He had injured his right groin when 27 years old and some swelling of the leg had followed.

A joiner aged 57 fractured his pelvis. Thrombosis and ulceration of the right leg followed. His mother had varicose veins and his brother an ulcer of the leg.

A farmer, when aged 22, had both legs severely bruised by a riding accident and varicose veins appeared. A year later Trendelenburg's operation was carried out bilaterally, marked swelling of the right leg occurring afterwards. At the age of 24 the varicose veins, which had reappeared, were injected with sclerosing fluid. Ten years later he fractured his right femur, the limb being immobilized for ten months with a plaster spica. Shortly after the plaster was removed the first ulcer appeared. The Wassermann reaction was negative. There was no family history of varicose veins or ulcers.

A labourer aged 58 had no family history of varicose veins or ulcers. When aged 27, while wearing puttees in the infantry, thrombosis occurred in the right leg with much swelling and aching. Varicose veins appeared for the first time, with ulceration, after a few months.

A Czech fur-cutter, a cigarette smoker, had suffered from thrombophlebitis migrans since the age of 21, with recurrent idiopathic thrombophlebitis of the superficial veins of the legs and right arm. No signs of arterial disease were present. There was marked venous stasis of the legs, with varicose veins. Ulceration first occurred when he was aged 31. His Wassermann reaction was negative and his weight 74 kg. His father and sister had ulcers of the legs.

#### 7. Silent Thrombosis

When a patient has venous stasis, with no history of thrombosis, a silent thrombosis may be suspected if there has been pulmonary embolism; otherwise it may be indicated by phlebography, by surgical exploration, or by post-mortem examination. In this series, in those patients with no history of thrombosis, phlebography was carried out in only one, and of the others some may have had a silent thrombosis.

*Illustrative Case.*—The mother of 13 children, weighing 82 kg., had bilateral varicose veins for many years, and these were injected when she was 42. Her sister had ulceration of the leg. There was no history of thrombosis at any time and she had never been in bed on account of illness of note or operation, nor had she suffered any injury. The Wassermann reaction was negative. The first ulcer appeared in the right leg at the age of 51. Nine years later a phlebogram showed blockage of the deep veins of the right thigh near the knee.

### Venous Stasis with No History of Thrombosis

In addition to the patient mentioned above there were others with no history of thrombosis.

#### 1. Venous Stasis due to Varicose Veins

There were 29 patients whose venous stasis and ulceration might have been due to varicose veins. Of these, 24 were women, of whom 17 were parous. In the whole group the family history of two was uncertain, but 17 of the remaining 27 gave a family history of varicose veins or ulcers of the legs or both. The age at which ulceration occurred varied from 20 to 78 years (mean 45.4 years). All but one had suffered from varicose veins for many years before ulceration appeared, and the problem arises whether these are cases of true varicose ulcer—i.e., ulcer due to varicose veins—or whether they are post-thrombotic, the thrombosis having been symptomless. Some of these patients had ulcers "riding" over a vein, to use the description applied by Homans (1939) to true varicose ulcers. The possibility of previous thrombosis in the other patients remains. The question of varicose ulceration is discussed later, but even were it assumed that most of the patients

in this group suffered from varicose ulceration they represent less than 11% of the whole series.

A tram driver weighing 84 kg., with a striking family history of varicose veins and ulcers of the leg, had varicose veins from the age of 12. An ulcer appeared on the right leg when he was 20 and on the left leg when he was 26. There had been no history suggesting thrombosis. Bilateral injection of varicose veins with sclerosing fluid was carried out when he was 20, and ligation and injection of the veins when 26, on both occasions after the ulcers had appeared. The veins were injected again when he was 29. The Wassermann reaction was negative. The early ulcers in this patient would seem to have been true varicose ulcers.

A mother of five children, who had been a baker, developed varicose veins at the age of 26 while bearing her first child. There was no family history of varicose veins or ulcers. One of the veins burst when she was 42 and an ulcer formed at the site. The varicose veins were treated by operation soon after with no benefit to the ulcer, and were injected when she was 50. Tremendous swelling of the leg resulted, no doubt due to a thrombosis of deep veins. She now has calcification of the varicose veins, much induration of the legs, and diabetes. Her weight is 76 kg.

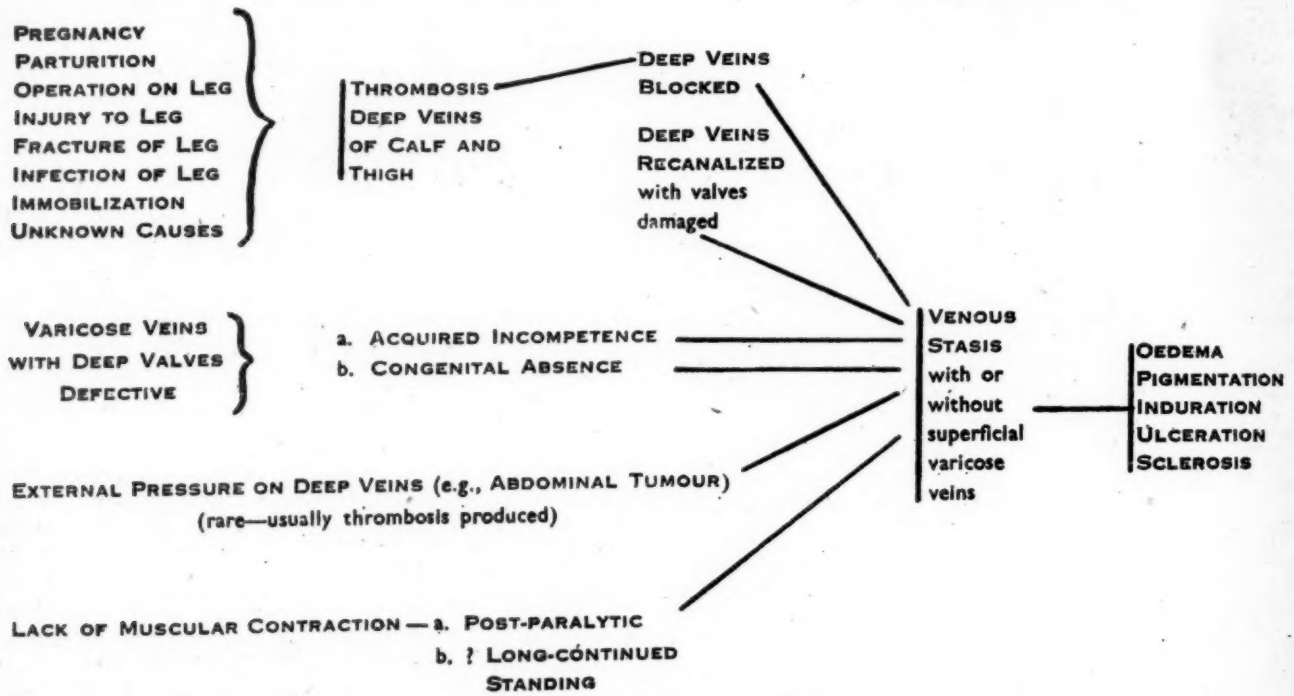


FIG. 2.—Causes of venous stasis in the lower limb.

### 2. Venous Stasis due to Miscellaneous Causes

A woman with congenital haemolytic icterus suffered from ulceration of the leg from the age of 17. Her mother and two sisters had ulcers of the legs.

A boot-repairer, whose mother had an ulcer of the leg, had suffered from acute anterior poliomyelitis as a child. His left leg was wasted and he wore a walking-calliper. A gravitational ulcer appeared when he was 26. No varicose veins were present and there was no history of thrombosis. The ulcer was probably due to venous stagnation caused by lack of muscular contraction in the leg.

## Discussion

The causes of chronic venous stasis, and hence of gravitational ulceration of the leg, are summarized in Fig. 2.

### Thrombosis of Deep Veins of the Lower Limb

This had been present in about 89% of patients in the series and seems to have been the most important cause of gravitational ulcer. The pathology of thrombosis will not be discussed here, as the subject has been fully reviewed by Allen, Barker, and Hines (1946), Zilliacus (1946), and Birger (1947). Causative factors may be slowing of the blood flow, alteration in the composition of the blood leading to an increased tendency to clot, and injury to the intima of the vein. The blood flow in a leg vein may be slowed by lack of muscular activity, by pressure on the vein from outside, and owing to defective venous valves. Thrombosis may take place with no apparent cause, as in 19 patients in this series.

Homans (1934) pointed out the importance of the deep veins of the calf as the site of origin of thrombosis in the lower limb. In two large series of cases of pulmonary embolism examined post mortem by Rössle (1937) and Neumann (1938) the calf or plantar veins were the site of thrombosis in the majority. This was confirmed by Putzer (1939), Frykholm (1940), Bauer (1941), and Hunter, Krygier, Kennedy, and Sneeden (1945). Only 10% of all thromboses in the femoral veins are not associated with deep thrombosis below the knee (Homans, 1943).

Thrombosis in the veins of the calf may cause pain and deep tenderness (Homans, 1934; Boyd, 1948), but often a "silent thrombosis" has been demonstrated in patients with pulmonary embolism (Homans, 1943) and by phlebographic examination (Bauer, 1941). The absence of any history of thrombosis in a patient with gravitational ulceration is therefore no evidence that the latter is not post-thrombotic in origin, and probably only by phlebography or dissection can the point be settled in a particular case. It is possible that some of the patients in the present series with no history of thrombosis had suffered from a "silent thrombosis."

Thrombosis originating in the lower part of the leg tends to extend centrally, often into the ilio-femoral vein. As a result of such thrombosis the venous return from the lower limb is impaired, as Gay (1868) observed, the lumen of the deep veins being occluded, though sometimes not

completely. Periphlebitis secondary to an aseptic inflammation of the wall of the veins (phlebitis) may be present (Bauer, 1948). Later, recanalization of the thrombosed vein may take place, but the valves are permanently destroyed (Homans, 1917; Edwards and Edwards, 1937; Bauer, 1948). This recanalization and valve destruction in the popliteal and femoral veins leads to marked venous stasis in the lower limb when the individual is erect. Linton and Hardy (1948) believe that ulceration of the leg does not take place until the thrombotic veins have become recanalized, and that this may take from one to 29 years from the time of venous thrombosis.

#### Varicose Veins

These may usefully be considered as primary or secondary. The primary type develops spontaneously and is probably due to inherited weakness in the structure of the vein—dilatation of the vein leading to incompetence of the valves (Edwards and Edwards, 1940)—or to congenital absence of valves as described by Eger and Casper (1943) and Curtis and Helms (1947). The secondary type develops as the result of thrombosis of deep veins in the lower limb (Meyer, 1932), though if the latter has been "silent" it may be difficult to distinguish this type from the primary. Post-thrombotic ulcers may be associated with such varicose veins of secondary type.

Do varicose veins of the primary type lead to venous stasis and ulceration? Varices may occur, as Meisen (1932) pointed out, with stasis and without stasis, and stasis may occur without varices (as in 31 patients in this series). The two may be independent. Clinical experience suggests that primary varicose veins, sometimes quite severe, occur not uncommonly without venous stasis. However, stasis and ulceration may be found with primary varicose veins, and the condition is well described by Bauer (1948). A family history of varicose veins is usual, a history of deep thrombosis is absent, women are affected twice as often as men, a bursting sensation is present in the legs on standing, oedema and other signs of chronic venous insufficiency are present similar to those following thrombosis, but phlebography and operative exploration differentiate the conditions. Bauer (1948) believes that idiopathic or non-thrombotic femoral incompetence, as he names it, is due to deficiency of the valves of the femoral and popliteal veins caused by phlebosclerosis affecting the deep veins, and not merely the superficial veins as in primary varicose veins, without evidence of venous insufficiency. Probably a similar result is produced by congenital absence of valves in the deep veins (Eger and Casper, 1943; Curtis and Helms, 1947).

Thus with primary varicose veins ulceration may be present if there is congenital or acquired absence or incompetence of valves of the deep veins. Ulceration may be absent if only the superficial veins are varicose. Thrombosis may occur, however, in the deep veins of patients with the latter condition, following treatment of the superficial varices, or may be due to any of the causes which lead to thrombosis in an individual without varicose veins. A post-thrombotic ulcer may result. In the present series primary varicose veins do not seem to have been a cause of ulceration in many patients, as only 32 (11%) gave no history of previous thrombosis. Three of these did not have primary varicose veins, and of the others some may have had a "silent" thrombosis.

Venous stasis due to complete absence of muscular contraction is rare, only one patient in the series having gravitational ulceration from this cause (previous anterior poliomyelitis), but comparative lack of movement while standing at work may be a secondary factor of note in some patients with ulcers.

#### Arterial Disease

Gay (1868) and Heller (1943) considered arterial disease to be an important cause of some chronic ulcers of the lower part of the leg. More recently Hines and Farber (1946) have described ulceration of the leg due to arteriosclerosis and ischaemia occurring in the presence of hypertensive disease, with no other vascular or cutaneous disease. Although in the present series no ulcer was thought to be due only to arterial or arteriolar disease, the high proportion of patients with hypertension suggests that this condition may be a factor in the aetiology of gravitational ulcers. Obliterative arterial disease may occur without a rise in blood pressure. The presence of an arterial factor in the causation of some ulcers may account for the beneficial effect of sympathectomy in certain patients (Borrie and Barling, 1948).

The treatment of chronic venous insufficiency and ulcers of the leg will not be discussed here, but it is clear that to be effective an accurate diagnosis of the cause and a knowledge of the aetiological factors involved are important.

#### Treatment

In this country at the present time the concentration on treatment of superficial varicose veins in patients with venous stasis is neither rational nor useful, and the results, as shown in several patients in this series, may be appalling. More often than not it is harmful, increasing the degree of stasis already present. Progress will be achieved only by a better understanding of the essential causes of the condition. Measures to prevent thrombosis are important, and when venous stasis has appeared the continued use of elastic supports to prevent oedema is essential. Various surgical techniques, such as those of Bauer (1948) and Linton and Hardy (1948), require consideration.

### Summary

A series of 270 patients with gravitational ulcer has been investigated. This type of ulcer results from chronic venous stasis of the lower limb. In 88.6% venous stasis was due to previous thrombosis of deep veins in the leg. Varicose veins may be present as a result of thrombosis, but primary varicose veins rarely cause venous stasis and gravitational ulcer. The futility of treatment of the condition by attention to superficial varicose veins is stressed.

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# A NEW NEONATAL SYNDROME

BY

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During the ten-months period December, 1946, to October, 1947, a new syndrome affecting infants appeared in the nurseries of the Birmingham Maternity Hospital. Eight cases were observed, the predominant feature being a circulatory disturbance in one or both lower limbs, while some cases in addition showed muscular weakness or palsy. The case incidence was sporadic, and on only one occasion was the interval between cases less than three weeks. The aetiology was unknown, and neither the medical nor the nursing staff could recall similar cases. Search for guidance in standard textbooks proved fruitless, and it was concluded that the syndrome must have been caused by some new factor, such as a new line of treatment, that had never before operated.

## Case Reports

*Case 1.*—On April 6, 1947, a 60-hours-old infant was found to have a flaccid paralysis of the right lower limb with apparently complete sensory loss below mid-thigh; the leg was pale and cold and no arterial pulsation could be detected. The appearance suggested an embolism of the common femoral artery, but the exact time of onset was uncertain. Next day the foot was still pale and cold, but the calf showed a mottled cyanosis and in a short time the whole limb became warm and flushed. Patches of local discoloration persisted on the front of the leg, the heel, and great toe, and desquamation was followed by scab formation and a chronic ulcer over the anterior border of the tibia. At 1 month old there was still a small unhealed ulcer, and considerable weakness in the anterior tibial group of muscles. At 2 years old there was a pes cavus, a limp, and poor dorsiflexion of the foot.

In an attempt to elucidate the aetiology the obstetric history was checked in detail. The mother, a primigravida, had been treated in hospital from the 34th to 38th week of pregnancy for pre-eclamptic toxaemia. Labour had been induced surgically, but after three days' inertia delivery had been effected by lower-segment caesarean section under general anaesthesia. The child was asphyxiated at birth, and was resuscitated with oxygen and an injection of nikethamide into the umbilical cord. It weighed 5 lb. 3 oz. (2.35 kg.). It had not been delivered through the incision by traction on one leg, and no injection was recorded as having been given into the buttock. The only conclusion that could be reached was that spontaneous thrombosis or embolism of unknown origin had occurred in the main artery to the limb.

It was then recalled by the ward sister that a somewhat similar though more severe case had occurred a few months previously, and that the child had subsequently died.

*Case 2.*—On consulting the records it appeared that a child had been delivered spontaneously on Dec. 14, 1946, following surgical induction of labour at 37 weeks for disproportion in a primigravida; the second stage of labour had been prolonged to three hours, and the child, weighing 6 lb. 9 oz. (2.98 kg.), had been born in a state of white asphyxia. Its condition being critical, nikethamide followed by lobeline and a second dose of nikethamide had been injected into the umbilical cord without any immediate effect. Six hours later the right leg was seen to be cyanosed and flaccid, with some oedema of the buttock, and during the next day it became cold and anaesthetic. Gangrene of the extremity developed and the infant died on the eleventh day from peritonitis. Necropsy showed thrombosis of the right common iliac artery and also of the inferior mesenteric vessels; there was gangrene and perforation of the sigmoid colon.

No common aetiological factor could be deduced from these two cases, although it seemed probable that the one was a more severe variant of the other. However, the next three months produced five more cases which, although not so severe, presented sufficient similarity to those preceding to warrant grouping together.

*Case 3.*—A child was delivered on April 30, 1947, by caesarean section for placenta praevia; a general anaesthetic was used. The child was sleepy and asphyxiated at birth, and three injections of nikethamide were given into the cord before respiration was established. On the second day the left buttock was found to be discoloured and indurated as though severely bruised; there was no concomitant paralysis, and the condition resolved in a few weeks without ulceration. It could easily have passed unrecorded had the previous cases not stimulated interest and observation.

*Case 4.*—This child was seen on May 25. Labour had been induced at 37 weeks in a primigravida with a posterior position of the occiput, but there was an interval of three days before the onset of labour. Intrauterine infection developed, and eventually a small infant 5 lb. 3 oz. (2.35 kg.) was delivered in a state of white asphyxia. Nikethamide was injected into the cord, and recovery was uneventful until the third day, when an area of discoloration was noticed on the right buttock. This area was indurated as though severely bruised, and the overlying skin became necrotic, to produce an unhealthy ulcer which healed with difficulty in about a month. There was never any demonstrable paralysis.

Two further cases were recorded within 24 hours of each other three weeks later.

*Case 5.*—A baby born on June 18 was the second child of a woman aged 47; during a difficult forceps extraction of a 9-lb. (4-kg.) infant there was considerable delay in delivery of the shoulders, and the child was born in white asphyxia. Two doses of nikethamide were injected into the umbilical cord. Twelve hours later there was extensive discoloration of the right buttock and right side of the scrotum, and during the next two days the gluteal skin broke down to form an ulcer, and a tense hydrocele developed. Movements of the right lower limb were greatly diminished, and there was temporary palsy of the anterior tibial group of muscles. The gluteal ulcer healed in a month, and leg and ankle movements gradually returned to normal.

*Case 6.*—The coincident case was less serious. Labour had been induced at 37 weeks for disproportion in a primigravida, and an infant weighing 7 lb. 3 oz. (3.26 kg.) was delivered with forceps for foetal distress; its condition was only fair, and one injection of nikethamide was given into the cord. Three

days later the typical indurated area of discoloration had appeared on the right buttock, and movements were diminished at the right ankle. There was no subsequent ulceration, and recovery was complete in 10 days.

*Case 7.*—This child was born on July 16. The infant was delivered precipitately through a rachitic flat pelvis after a long delay at the brim, and its condition was so poor that cerebral haemorrhage was presumed. Its life was twice despaired of, but after three separate injections of nikethamide into the cord respiration was more or less established. Six hours later the child was still cyanosed. There was discoloration of the legs : the left showed a mottled cyanosis of the buttock, thigh, and flank, while the right was pale, atonic, and inactive ; there was also oedema of the left side of the scrotum. Within an hour the pallor of the right limb had been replaced by deep cyanosis, but the child died within 24 hours and no further changes were recorded. Necropsy revealed cerebral haemorrhage and atelectasis with no demonstrable thrombosis or embolism in the main arterial tree of either lower extremity.

Following this case a tentative diagnosis was propounded, and it was hoped that further cases might be avoided. However, the arrival of a new resident two months later was followed by the eighth and final case.

*Case 8.*—This child was born on Oct. 1, 1947. Caesarean section had been performed on account of some disproportion and inertia, and the child's condition was poor enough to require nikethamide for resuscitation. Within seven hours the left buttock was cyanosed and mottled, the left side of the scrotum was discoloured, and the left leg was pale and atonic (see Fig.). The leg regained full movement within a few days, but the gluteal skin broke down to produce an ulcer, which healed in a few weeks.

Case 8. The area of discoloration of gluteal and scrotal skin is limited almost exactly by the midline of the body. The marks on the lateral aspect of the right buttock have been produced by pressure from the napkin on which the infant was lying.

## Discussion

To summarize these eight cases, we have a neonatal condition that has apparently not been previously recorded ; it is probable that cases of little severity have escaped notice in the past, and in fact search in the hospital records has disclosed reference to one such case in 1945. The chief characteristics include the onset of vascular disturbances shortly after birth in one or both lower extremities, with a predilection for the gluteal region, and sometimes a flaccid paralysis of the limb. In one infant there was a fatal issue from cerebral haemorrhage ; in another the inferior mesenteric vessels were affected and the child died from peritonitis ; in a third there was residual paralysis of the anterior tibial group of muscles. All the remainder recovered fully.

After the occurrence of the seventh case a determined effort was made to establish a diagnosis, and various theories were put forward. The unilateral bruising of the buttock suggested thrombosis or embolism of the inferior gluteal artery, which in foetal life represents the main arterial axis of the lower extremity. It is the chief branch of the hypogastric, which continues as the umbilical artery ; the external iliac artery is very much smaller. The inferior gluteal artery contributes the chief blood supply to the sciatic nerve. Embolism was considered improbable on account of the bilateral effect in Case 7 and the mesenteric lesion in Case 1. No cause could be adduced for a primary arterial thrombosis. Injection of vitamin K into the infant's buttock was disproved. The obstetric procedures were so diverse, including spontaneous, forceps, breech, and caesarean deliveries, that there seemed small chance of finding a common factor. However, it was observed that all infants had been born in a state of white asphyxia, and all had required at least one injection of nikethamide for resuscitation. Speculation was aroused upon the possibility of an intravenous injection being responsible for an arterial lesion, when it was suddenly realized that in all probability the injection had been given on occasion into an umbilical artery.

The resuscitation of the newborn is always an emergency procedure, and if it should follow operative delivery the obstetrician may still be engaged in the treatment of the mother. In consequence, the anaesthetist or a junior hospital resident may be instructed to inject " nikethamide into the cord," by which it is intended that 0.5 to 1 ml. of nikethamide shall be injected into the umbilical vein and milked down the cord to the umbilicus. Instead of the familiar engorged cord with a prominent distended vein and two smaller encircling arteries, there will probably be a practically avascular structure in which two dark vessels are dimly discernible. The operator, unfamiliar with the appearance of the cord in states of shock, and anxious to discharge his duty rapidly, may select a vessel and puncture it with difficulty ; whichever he selects will be wrong, for the vein is empty, transparent, and practically invisible, and the injection will have been made into an artery.

It is my belief that in the past this accident has been by no means uncommon, and that the production of a pathological lesion depends upon three factors. The volume of injected fluid and the vigorous nature of the " milking " process will determine how much nikethamide enters the foetal hypogastric arteries, while the height of the infant's systolic blood pressure will decide how far the retrograde injection advances before being swept peripherally in the arterial stream. The actual pathology might be an arterial spasm with ultimate thrombosis similar to the condition in the upper extremity following accidental intra-arterial injection of anaesthetic solutions. The occurrence of a bilateral case may be explained by the use of both umbilical arteries, while the massive effect in Case 1 followed a triple injection —enough to fill the common iliac artery and overflow into the aorta and inferior mesenteric. It is hardly surprising that the notes record " no immediate improvement."

It may be argued that the above hypothesis is mere conjecture supported by circumstantial evidence, and it must be admitted that proof is still lacking. An attempt has

been made to demonstrate the relevant arterial distribution by injecting methylene blue into the umbilical artery of a living anencephalic foetus, but without success. Experiments have been made elsewhere to reproduce the lesion in cats, but no positive result has been obtained. The difficulty of such experiments lies in the fact that the injection must be made against the full force of the neonatal blood pressure, and the fluid is thus unlikely to travel so far in a retrograde direction as it would when the subject was shocked or gravely asphyxiated. However, it is of some significance that after explanation of the danger of intra-arterial injection to the resident staff no further cases were recorded; and those who are uncomfortably aware of having themselves made such an injection testify to the extreme facility with which it may be made in moments of stress and shortage of sleep. There is no satisfactory explanation of the variable interval between injection and discovery of the lesion (6–60 hours), and an inexplicable fact is the sudden appearance of this series of cases in a hospital in which the use of nikethamide by injection into the umbilical cord has been an integral part of the routine for neonatal resuscitation for several years.

**Summary**

A new syndrome is described, comprising arterial lesions with occasional paralysis in the lower limb of the newborn.

Eight cases are recorded as having occurred in a period of 10 months at a busy maternity hospital.

The aetiology of the condition remains unproved. It is suspected that the lesions may be due to injection of drugs into an artery in the umbilical cord. The evidence in favour of this theory is discussed.

I am deeply indebted to Dr. Frances Braid for her interest in these babies and her stimulating encouragement. I wish to thank Dr. Hudson, of the Walton Hospital, Liverpool, for details of a similar series of cases, and the staff of the Birmingham Maternity Hospital, under whom the cases were admitted, for permission to publish.

A number of Government scholarships have hitherto been available to selected nurses who wished to train as nurse tutors. The assistance given has covered the training and examination fees and the cost of books, and provided an allowance of £150 for the period of training. The Ministry of Health has decided to end this arrangement and to substitute the following. Nurses, both male and female, who are accepted by training institutions for training as nurse tutors should be granted leave on full pay, including emoluments where appropriate, for the period of the training. The nurse would be required to pay the full cost of the training, including examination fees and books. The courses cover an academic year and begin in the latter part of September or early October. The recognized institutions which will be running courses next term are: Battersea Polytechnic, Battersea Park Road, London, S.W.11 (40 places); King's College of Household and Social Science, Campden Hill Road, London, W.8 (20 places); Royal College of Nursing, 1A, Henrietta Place, London, W.1 (36 places); University College, Hull (12 places). The fees for the courses vary from £20 to £50. Applicants must (*a*) be registered in the General Part of the State *Register*, or the Part of the *Register* for Male Nurses (General Trained); (*b*) have had at least three years' experience in nursing in hospital since registration in any Part of the *Register*, including at least one year as a ward sister (or corresponding rank in the case of a male nurse) in an approved training school; (*c*) satisfy the training institution that their general education is such as to justify taking up training. Where an applicant is registered both as a general trained nurse and as a mental nurse or nurse for mental defectives, but has not had a year's experience in charge of a ward, the applicant must have post-registration experience, satisfactory to the General Nursing Council, in an approved training school for a period of at least four years.

# TETRAETHYLTHIURAMDISULPHIDE* IN THE TREATMENT OF ALCOHOLICS

BY

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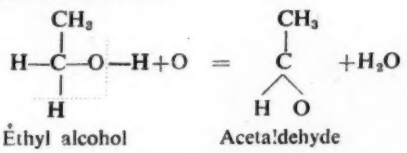
So numerous have been the drugs and techniques used and abused in the age-long struggle against alcoholic excess that one naturally is wary about recommending any new preparation. Yet tetraethylthiuramdisulphide, with the structural formula of $(C_2H_5)_2.N.C(=S).S.S.C(=S).N(C_2H_5)_2$, recently introduced by Dr. Erik Jacobsen, of Copenhagen, shows such promise that it merits extended trial so soon as it becomes readily available to the medical profession in this country. Adequate samples were placed at my disposal upon request, and the following preliminary report shows the advantages derivable from its administration.

## The Drug's Action

Before relating these it will be of interest to expound the pharmacological basis of the drug's action. For many years it has been known that certain substances—e.g., cyanamide and the fungus *Coprinus atramentarius*—though innocuous to man when taken alone, yet gave rise to unpleasant symptoms when alcohol subsequently was consumed. Tetraethylthiuramdisulphide has a similar action, and the work of Dr. Jacobsen and his colleagues in Copenhagen has shown fairly conclusively that these characteristic effects are due to an interference with the normal metabolism of alcohol in the body, so that unusually high levels of acetaldehyde become present in the blood stream. Acetaldehyde is a normal intermediate stage in carbohydrate metabolism, and after alcohol its presence in the blood shows a temporary slight increase. When any member of the sensitizing group of substances now under discussion has been taken before the consumption of alcohol the blood acetaldehyde rises steeply (up to tenfold) and its elimination is slow.

Aldehydes are derived from the simple oxidation of primary alcohols, as is shown by the following equation with structural formulae:




Ethyl alcohol Acetaldehyde

Exactly how tetraethylthiuramdisulphide interferes with the normal metabolism of alcohol is not yet known, but there is an interesting correlation between this and the course of events in vitamin $B_1$ deficiency. In the latter case pyruvic acid, not acetaldehyde, is the stage at which metabolism goes wrong. Aldehydes and ketones are closely allied, having the same general formulae $C_nH_{2n}O$. Similarly the aldehydic and ketonic acids are closely related, and pyruvic acid, $H—\underset{H}{\overset{H}{C}}—\underset{O}{C}—C\langle^{O}_{OH}$, is the simplest of the ketonic acids. Later the relation between the mechanism of the two derangements in carbohydrate metabolism will probably be discovered. Possibly some similar if not identical inborn

*This drug has the proprietary names of "antabus," "antabuse." and "antalco."

error of metabolism will be found to account for the hypersensitivity of certain individuals to small doses of alcohol.

Tetraethylthiuramdisulphide has an advantage over other sensitizing drugs in that, though its action is prolonged, lasting several days, there is no evidence of cumulative toxic effects in the dosage usually employed. Moreover, it is easy to carry and to administer orally in tablet form. No symptoms arise unless and until alcohol also is ingested. Then typical symptoms begin with a burning sensation in the face. This is followed by injection of the conjunctival vessels and redness of the face. The loose tissue around the eyes becomes congested and the patient may have difficulty in keeping his eyes open. The pulse increases in frequency and may gradually rise to 150 a minute, but there is little if any change of blood pressure, though most patients complain of a pounding at the heart. Giddiness, hammering in the ears, and headache are next to appear, and the patient complains of a vague generalized anxiety and distress. Finally, if the doses of both substances have been large, he vomits and feels "thoroughly ill." Symptoms begin within a quarter of an hour of the intake of alcohol and last a variable time (up to five hours), then fade away gradually in sleep. On the following day the patient feels lackadaisical and listless, but is capable of carrying on his work.

These typical symptoms, of course, are subject to considerable individual variation in their march and severity, but the above recital affords a general picture of the average patient under close observation. Advantage has in two ways been taken of the disagreeable sequelae of this drug plus alcohol as an aid in the total treatment of excessive drinkers.

### Method of Treatment

First, in a special institution for the rehabilitation of alcoholics those patients allowed out on parole receive a dose of 1 g. the previous day and 0.75 g. at breakfast on the morning of the day of *congé*. As a knowledge of the effects of the drug has not yet spread abroad patients do not know the consequences which a breaking of parole will entail. They think that the tablets received are merely vitamins, to which they are accustomed. Should a patient upon his return from an outing complain that queer things befell him his physician draws the obvious conclusion, but, instead of asking awkward questions, explains that the susceptibility of persons under treatment is such that any lapse to alcoholic beverages is likely to be fraught with not unmerited distress.

As patients and public become knowledgeable concerning the properties of these innocent-looking tablets this particular device will cease to have strategic value and the second method must be adopted.

This method is frankly to discuss with the patient the way in which tetraethylthiuramdisulphide can be used to contribute to a cure in his individual case. He is then free to decide whether to co-operate in the plan. Though there is no pretence that the drug of itself can rectify the defective personality structure of which alcoholism is a symptom, it can, by temporarily rendering the lure of alcohol easier to resist, gain a sober interval in which the process of reorientation can be begun. Possibly also, though this is at present not proved, a small daily dose in a patient of good will may establish a permanent distaste for alcohol. Even so, unless those underlying motivations which prompted the patient to excess be adjusted he cannot be regarded as cured. The largely unconscious urges which gained neurotic gratification via alcohol will, if this means of escape be denied to them by pharmacological force alone, break out in some other and possibly more objectionable form. This drug is therefore not recommended as a quack cure, but as a powerful addition to our already existing therapeutic armamentarium.

Before regular administration of tetraethylthiuramdisulphide is begun the patient should be put to a clinical test as follows. After sensitization has been established in the way about to be described, alcohol is administered to the patient according to his usual habit when drinking. His reactions then are carefully studied throughout. The detailed recital of a single typical but rather severe case will be more instructive than any attempt at statistics in illustrating the method adopted during a course of general and psychological treatment.

### Illustrative Case

A married man aged 42, with no children, was first admitted in 1947. He was a Cambridge graduate and barrister-at-law, teetotaller until the age of 25, when he began drinking, which rapidly became excessive. His behaviour towards his wife became so brutal that he eventually consented to undergo institutional treatment. Under this he improved and gained considerable insight. He had, however, a suspicion, not altogether unfounded, that his wife meant to leave him when he got cured, and while he was undergoing treatment was only keeping in touch with him from a sense of her moral duty. He showed all the signs of an overcompensated inferiority complex with an overwhelming wish to be in the limelight and the "life and soul of every party."

On his return home renewed quarrels with his wife soon led to relapse. He thereupon left home and took up quarters in a public house at a port, where he drank heavily. While thus disporting himself he received a severe blow on the head in a drunken brawl. This necessitated trephining for removal of a blood clot. After discharge from hospital he went home and for a time refrained from alcohol. Then, without knowing why, he relapsed and kept drinking up to a bottle of gin a day and had superadded acute exacerbations associated with amnesia.

He insisted, however, that he had no real desire for alcohol but wanted to be cured of his uncontrollable habit. His history was already known in detail, as he had by request written an autobiography during his first admission, and this was brought up to date when he of his own wish returned for treatment early in 1949. The advantages derivable from tetraethylthiuramdisulphide were then explained to him, and he readily promised his whole-hearted co-operation. After a few days' rest, sedation, and detoxication a first test with the drug was performed to gauge his individual reactions. A dose of 0.75 g. was given one evening, and was repeated next morning. At 2.30 p.m. he was given a "double" gin (2 oz. (57 ml.) of 70% proof alcohol). Ten minutes later his face became hot and red. His conjunctivae were bloodshot and his lower eyelids puffy. His pulse went up from 68 to 120. Respiration also increased and he complained of a pounding at the heart and in the head. At 2.50 p.m. another double gin was given. Within a few minutes the patient's distress increased, his pulse rose to 130, and he felt so squeamish that he was sure any more gin would make him sick. These symptoms gradually subsided and he felt normal in just over two hours.

That night 1 g. of the drug was taken, and again at 10 a.m. the next day. At 3.45 p.m. he was given 2 oz. of gin. Symptoms as previously described came on more quickly than on the first occasion. A second 2 oz. of gin was given at 3.55 p.m. By 4 p.m. he felt extremely uncomfortable, with all symptoms increasing in severity. He next complained of seeing double and feeling generally ill and confused. At 4.05 p.m. a third 2 oz. of gin was given. (This order of drinking was the man's usual, and without the drug did not upset him, but led to more drinks.) After this third gin he became rapidly confused and felt desperately ill and anxious; pulse 150, respirations 36. Tingling followed by anaesthesia of the left hand developed and he could not move his left ring-finger and little finger. (These latter unusual symptoms probably are associated with his cranial operation.) At this point his face became pale instead of red, and he complained of feeling cold. At 4.25 p.m.

he vomited and asked to be allowed to go to bed. He complained of "noises in his head as if an engine were pumping away outside." At 5 p.m. he became sleepy and refused a proffered cup of tea and a cigarette. At 5.40, 5.45, and 6 p.m. he again vomited and complained that the vomit tasted unusually acid. He also felt "icy cold" but otherwise better. At 8 p.m. he vomited for the last time, and thereafter slept fitfully through the night.

Next morning he "felt a bit washed out" and "uneasy in the stomach," but he worked in the garden for two hours, morning and afternoon, as usual. Three days later, according to a previous arrangement, he travelled home (a long journey with two changes and waits, involving a three-days absence) to attend a meeting of directors, before, during, and after which he used on former occasions to indulge freely in drink. On this occasion he was primed with tetraethylthiuramdisulphide, 0.75 g. night and morning over the period. He did not experience any disagreeable symptoms and did not have any inclination to drink. His institutional treatment will shortly be terminated. Then, as an added precaution when in the outer world, a daily dose of 0.25 g. will be prescribed for a month or two with a view to giving him an added sense of security, as it has done to others.

### Comment

There is a hope that in milder cases, with the help of tetraethylthiuramdisulphide, the patient may receive enough help and understanding from his environment to dispense with specialized institutional treatment, or at any rate to shorten its duration. This, however, will require careful judgment, and remains for future experience to evaluate. At present one is justified in considering that tetraethylthiuramdisulphide seems likely to occupy a useful place in the treatment of alcoholics, and that it merits extensive but cautious investigation. The reactions of each individual patient under his usual drinking habit should be carefully tested the day after an initial sensitizing dose of the drug. Under out-patient conditions vigilance is required to see that a patient who has been placed on a small regular dose of the drug is not also managing to consume some alcoholic beverage. Should he do so the dose ought immediately to be quadrupled.

### Summary and Conclusions

The use of tetraethylthiuramdisulphide is recommended as a useful ancillary, but not as a substitute for, general and psychological methods in the treatment of alcoholics.

The pharmacological action of the drug is discussed. It is innocuous to man unless followed by alcohol, but certain precautions in its administration are advocated.

Details in a severe case of alcoholic addiction are related in order to illustrate the symptoms and technique in treatment.

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Among developments that Governor Dewey has recently announced will be carried out in the New York State mental hygiene programme (*New York Times*, July 20) is the establishment of a new relationship between voluntary hospitals and State mental hospitals; the former will provide preliminary treatment for patients before they become State charges. A second innovation that he described as "my own private brain child" is the creation of a new intern system in which 200 men yearly will serve for two years as interns in every State mental hospital, which would pay interns more than the voluntary hospitals do. "This is a system of which I vigorously disapprove," he said, "unless it is a public necessity, and I think this is a public necessity."

# INCIDENCE OF PHYSICAL DISORDERS AMONG PSYCHIATRIC IN-PATIENTS

## A STUDY OF 175 CASES

BY

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During my period of duty as resident medical officer to the psychiatric unit I was so impressed by the number of patients needing attention for physical conditions that I reviewed the case records of all those admitted to the unit in 1948 in order to estimate the frequency of such conditions among the patients treated and the relevance of these to their psychiatric conditions.

### Material Studied

During 1948 the unit had the use of 28 beds—22 for females and six for males, though, owing to redecorations, not all the former were continuously available. A total of 179 patients were admitted, of whom four did not stay long enough to allow of full examination and so are excluded from this series. The number of patients studied was 175, comprising 124 women and 51 men. All were in need of psychiatric attention, and no purely physical criterion entered into their selection.

The predominant features of the psychiatric conditions found were as follows: affective reactions, 108 (endogenous depression 51, reactive depression 35, anxiety states 16, cyclothymic reactions six); hysterical reactions, 22; schizophrenic reactions, 20; obsessional reactions, 16; organic reactions, five; hypochondriasis, neurasthenia, behaviour disorder, and drug addiction, one each.

### Abnormal Physical Conditions

In no fewer than 77 patients (44%) some physical condition needing attention was found. As might be expected, the incidence was higher in those over 40 than in younger patients (61% against 35%).

In four patients serious physical disorders were first discovered during examination in the unit, their presence not having been previously suspected; these comprised one case each of pulmonary tuberculosis, bronchial carcinoma, glioma, and major epilepsy. In two other patients serious physical disorders, not related to the psychiatric condition, developed during their stay in hospital; these comprised one case each of cerebral thrombosis and thrombophlebitis.

In the accompanying tables the various physical conditions found are analysed according to their apparent relevance to the psychiatric conditions for which treatment was required.

TABLE I.—*Physical Conditions Contributing to the Onset of Psychological Illness*

| | No. of Patients |
|---|---|
| Gynaecological conditions (menopause, 6; pregnancy, 4; eclampsia, abortion, sterilization, puberty, 1 each) | 14 |
| Disorders of central nervous system (epilepsy, 3; cerebral contusion, glioma, internal carotid aneurysm, poliomyelitis, encephalitis lethargica, 1 each) | 8 |
| Disorders of respiratory tract (influenza, maxillary sinusitis, asthma, pulmonary tuberculosis, bronchial carcinoma, 1 each) | 5 |
| Orthopaedic conditions (prolapsed intervertebral disk, 2; fracture of tibia, 1) | 3 |
| Disorders of vision (cataract, Leber's atrophy, 1 each) | 2 |
| Endocrine disorders (acromegaly, hypothyroidism, 1 each) | 2 |
| Arteriosclerosis | 1 |
| Chronic nephritis | 1 |
| Intestinal obstruction | 1 |
| Otosclerosis | 1 |

TABLE II.—*Physical Disorders Resulting from Psychological Illness*

| | No. of Patients |
|---|---|
| Lesions resulting from suicidal attempts (of which 4 occurred before admission) | 6 |
| Asthma | 1 |
| Collapse of lower lobe of left lung | 1 |
| Physical sequelae of anorexia nervosa | 1 |
| Stomal ulcers | 1 |

TABLE III.—*Physical Conditions Not Apparently Related Aetiologically to Psychological Illness, but Requiring Attention*

| | No. of Patients |
|---|---|
| Disorders of central nervous system (epilepsy, 2; frontal lobe injury, cerebral thrombosis, narcolepsy, migraine, ataxia of unknown cause, tremor of unknown cause, 1 each) | 8 |
| Disorders of alimentary tract (dental conditions, 6; stomal ulcers, 2) | 8 |
| Disorders of respiratory tract (pulmonary tuberculosis, 3; emphysema, maxillary sinusitis, tonsillitis, 1 each) | 6 |
| Gynaecological conditions (pregnancy, cervical polyp, cervical erosion, retroversion of uterus, pruritus vulvae, 1 each) | 5 |
| Disorders of veins (varicosity, 2; thrombosis, phlebitis, haemorrhoids, 1 each) | 5 |
| Endocrine disorders (thyroid adenoma, 2; diabetes mellitus, hypothyroidism, 1 each) | 4 |
| Orthopaedic conditions (cervical rib, scoliosis, pes cavus, 1 each) | 3 |
| Anaemias | 3 |
| Hernia | 2 |
| Skin conditions | 2 |
| Rheumatoid arthritis | 1 |
| Detached retina | 1 |
| Otitis media | 1 |
| Chronic mastitis | 1 |

*Laboratory Investigations.*—The number of patients showing abnormal findings from laboratory and radiological investigations are as follows:

| | | | |
|---|---|---|---|
| Electroencephalography | 13 | Cerebrospinal fluid | 2 |
| Serum cholesterol | 5 | Blood urea | 2 |
| Chest radiograph | 4 | Basal metabolic rate | 2 |
| Skull radiograph | 4 | Ventriculography | 1 |
| Fractional test meal | 3 | Bronchography | 1 |
| Blood counts | 3 | Electrocardiography | 1 |
| Blood sugar | 3 | Blood Wassermann or Kahn | 1 |
| Barium meal or enema | 2 | | |

*Summary of Findings.*—Out of the 175 patients, 77 (44%) presented some physical condition requiring attention. Of the 10 patients (6%) whose physical condition resulted from psychological illness, there were six in whom the physical lesion was consciously induced in a suicidal attempt. In the other four the physical condition found had a definite psychogenesis. In 39 patients (22%) the physical condition was considered to contribute to the development of the psychological illness. In 26 patients (15%) the physical and psychiatric conditions did not appear to be aetiologically related.

## Discussion

The importance of the psychiatric aspect in many patients suffering from undoubted organic disease is now widely recognized, and is reflected in the development of the concept of psychosomatic medicine. This has perhaps led to less emphasis being laid on the physical factors in psychiatric syndromes, especially in those which are not obviously of organic type. The figures given above indicate the importance of this aspect of psychiatry. That this may be underestimated in general wards as well as in psychiatric wards is indicated in a study made by Comroe (1936). He followed up 100 patients who after admission to a medical clinic were diagnosed as suffering from neurosis, and found that 24% of them had definite organic disease within an average period of eight months, and that in most of them evidence of the organic disease was present during the original admission to the clinic.

The variety and gravity of physical disorders present among patients attending for psychiatric treatment are illustrated by the three case histories quoted below.

*Case 1.*—Man aged 72. A case of endogenous depression with a history of three depressive illnesses in the last 16 years. No physical symptoms, and no abnormal physical signs except glycosuria. A glucose-tolerance test indicated a moderately severe diabetic condition, the patient needing stabilization on insulin as well as electric convulsion therapy for the depressive condition.

*Case 2.*—Man aged 45. Referred for investigation of attacks of dizziness and fainting, which his doctor was satisfied "were not organic in the main," and a single epileptiform fit a few days previously. The doctor added that the patient had always had some worry—about his job or his mother's health or his own impotence. The left arm had been amputated many years ago following an accident. The clinical findings after admission were summed up thus: "A bad family background and a long history of gastric trouble, probably of emotional origin; evidence of an overconscientious obsessional driving personality. A history of disturbances of consciousness for seven to eight years; these have ranged from transient attacks lasting from a few seconds to a minute, in which he feels his actions are mechanical, to complete loss lasting as long as an hour and followed by vomiting. No physical signs, but sensory disturbances in a phantom left hand may have an organic basis. In the last nine months he has been lacking in libido, has become anxious and depressed, and feels that he is irritable and less efficient than before." After electroencephalography, skull radiographs, and ventriculography a diagnosis was made of glioma in the right frontoparietal region, and the patient was referred for deep *x*-ray therapy.

*Case 3.*—Man aged 29. Referred on account of three fugues during the previous 18 months. He complained of headaches and dimness of vision in the left eye, and was stated to have become apathetic and irritable since a subarachnoid haemorrhage eight years previously. Skull radiographs showed a shadow having the appearance of a large calcified aneurysm at the bifurcation of the left internal carotid artery. There were a few rales at the bases of both lungs but no other physical signs and no symptoms referable to his chest. The E.S.R. was 40 mm. in one hour. Radiographs of the chest showed extensive infiltration of both lungs with cavitation, and the sputum contained tubercle bacilli.

Full medical and surgical facilities are clearly necessary for the satisfactory treatment of such cases as these. The modern mental hospital is admittedly provided with such facilities, but there are many psychiatric patients for whom admission to a mental hospital is undesirable, particularly in view of popular prejudice and misinformation. Henderson and Gillespie (1944) state: "Recent experience has shown that with modern methods of treatment a considerable range of mental illness can be treated in the wards of a general hospital; but this is on the whole to be regarded as a provisional arrangement pending the establishment of specially constructed and equipped clinics within general hospitals." Treatment in such a unit is not merely a matter of investigation and transfer elsewhere, and the average duration of stay of a patient there is comparable to that in a general ward (Sands, 1948). At this time, when so much hospital planning is taking place, it may not be inappropriate to call attention to the need for such psychiatric units, as exemplified by the facts quoted in this paper.

## Summary

The incidence of physical disorders among 175 patients admitted to a psychiatric unit is analysed. In 44% the physical condition required attention. In 22% a physical condition contributed to the psychological illness; in 6% a physical disorder resulted from the psychological illness; in 15% physical and psychiatric disorders occurred together but were not apparently related aetiologically.

The importance of full physical investigation of all psychiatric patients is emphasized. The need for properly equipped psychiatric units in general hospitals is stressed.

I am indebted to Dr. Desmond Curran and Sir Paul Mallinson for their help in the presentation of this paper and for permission to

quote from the records of patients under their charge, and to Dr. J. B. Randell, Dr. H. F. Osmond, and Dr. L. Ford for their help.

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# FAMILIAL PERIODIC PARALYSIS

## REPORT OF A CASE

BY

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Familial periodic paralysis presents a well-defined clinical picture. It was first described by Cavaré (1853), whose findings have been supplemented by studies of the electrocardiogram (Janota and Weber, 1928), of the electroencephalogram (Watson, 1946), and of rare features such as non-familial incidence, protracted seizures, visceral involvement, and fatal complications (Smith, 1939). Precipitation of attacks has been ascribed to physical exertion and mental strain, indulgence in carbohydrates or alcohol, alimentary disturbance such as overeating, hunger, diarrhoea, or constipation, and exposure to cold or damp. Postulated relationships between this and other conditions —e.g., endocrinopathy (Shinosaki, 1926), migraine (MacLachlan, 1932), muscular dystrophy (Biemond and Daniels, 1934), spinal vascular spasm (Vernon, 1936), chemical defect of the neuraxis (Pudenz, McIntosh, and McEachern, 1938)—are inconstant and indefinite.

The search for an adequate pathology was initiated by suspicion that muscular metabolism was deranged by some transitory autotoxaemia, which was suggested by arrest of gastric digestion and motility during the palsy (Mitchell, Flexner, and Edsall, 1902), and by transient urinary anomalies—e.g., acetonuria (Pastine, 1918), albuminuria (Shinosaki, 1926), and creatinuria (Ferrebee, Atchley, and Loeb, 1938). Recent studies of the blood chemistry of this syndrome have led to a fundamental advance in the state of knowledge as it existed between the review of the literature made by Singer and Goodbody (1901) and that by Schoenthal (1934).

From a casual observation that the potassium content of the blood serum was lowered during the palsy (Biemond and Daniels, 1934) there developed a new line of inquiry (Walker, 1935). A low serum potassium was found in attacks induced by administration of glucose in large quantities and insulin, separately and together (Aitken, Allott, Castleden, and Walker, 1937), and by adrenaline injection (Allott and McArdle, 1938). Attention has been drawn to alterations in the phosphorus balance of the blood (Milhorat, 1937; Allott and McArdle, 1938), variations in electrolyte features of the blood (Ferrebee *et al.*, 1938), and experimental evidence suggestive of a central controlling factor (Pudenz *et al.*, 1938). The pathogenesis of this disease presumably depends upon an excessive call for potassium in the muscles, its consequent withdrawal from the blood and retention in the body, with parallel changes in phosphorus metabolism. Undue lability of the serum potassium and phosphorus in relation to sugar mobilization perhaps conditions some motor dysfunction, such as interference with transmission of nerve impulses or inhibition of the muscular contractile response.

It has long been recognized that this palsy may be averted or arrested by the ingestion of various potassium salts—e.g., the acetate (Singer and Goodbody, 1901), the carbonate, the chlorate (Mitchell *et al.*, 1902), the bromide (Holtzapple, 1905), the chloride (Aitken *et al.*, 1937), the citrate (Herrington, 1937), and the phosphate (Allott and McArdle, 1938). The success of prophylactic potassium medication at night (Allott and McArdle, 1938) is probably related to nocturnal lowering of serum potassium in this malady (Gammon, Austin, Blithe, and Reid, 1939). Symptoms have been controlled also by choline esters (Pudenz *et al.*, 1938), pilocarpine (Guttmann, 1931), and pancreatic extract (Vernon, 1936), and averted by cod-liver oil (G.D.H., 1948).

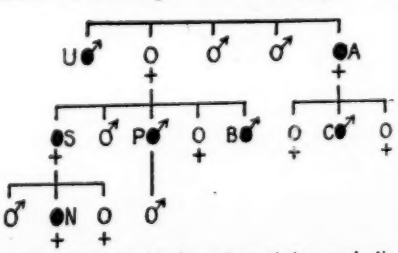
The following case, which illustrates typical familial and clinical features of this rare and remarkable malady, shows a prominent association between muscular exertion and paralytic seizures, a striking hemiplegic distribution of symptoms, and a prompt response to potassium therapy.

### Case Report

A South Indian male, aged 24, of a rice-eating race, serving in a labour corps in Ceylon, was referred for neuropsychiatric examination with a history of transient flaccid hemiplegic seizures occurring early in the morning after a hard day's work. A provisional diagnosis of hysteria had been suggested by the relation of these attacks to heavy work, their transitory duration, apparent response to bromides, irregular recurrence, and increasing frequency.

*Personal History.*—Symptoms had originated at the age of 17 with transient weakness of the lower limbs after strenuous work. As increasing frequency and severity of the disability began to interfere with his work as a cultivator, he had sought *ayurvedhic* treatment (herbals and massage), with apparent relief for several months. After resuming work, however, several relapses compelled him to abandon manual labour and obtain light work in a rural grocery store. This was followed by freedom from the disability. Enlistment in the Indian Army, six months before the time of examination, had been followed by another recurrence of symptoms, this time ranging in intensity from fleeting muscular weakness to profound loss of power lasting 2½ days. The frequency of attacks had increased from one in six to eight weeks to one in two to three weeks, having almost always affected both limbs of the right side, rarely having spread to the opposite side, and never to the trunk, neck, or head. The palsy evidently used to come on insidiously during sleep at night, as it would become apparent on awaking next morning without any premonitory warning. Spontaneous recovery had been the invariable termination of these seizures. Other past illnesses comprised two attacks of intermittent fever suggestive of malaria, and a few diarrhoeic episodes.

*Family History.*—Six other members of the patient's family, who were of coolie or labourer stock, had been afflicted by disabilities similar to his own, as indicated in the accompanying family tree. A maternal uncle, U, had suffered from occasional paralysis of his legs until his death, by accident, at the age of about 40. A maternal aunt, A, had had intermittent loss of power of her legs, but had gradually become free of her disability after about 25 years. This woman's son, C, was subject to paralytic attacks in his right arm and leg. The patient's elder sister, S, used to suffer from intermittent loss of power of her upper limbs, and one of her daughters, N, had a similar weakness of her legs. The patient's younger brother, B, had died in childhood during a para-




Members of family affected by periodic paralysis are shown in black.

lytic seizure of all four limbs and body. The patient, P, had been married for about three years. His only child had died of convulsions eight days after birth, but had exhibited no manifestations of paralysis. No information was available regarding the patient's maternal grandparents. No paralytic disability was known to have occurred in his father's family.

*Investigations.*—Observation in hospital for a fortnight revealed no physical abnormality; the urine, faeces, blood, and spinal fluid were normal. Psychiatric investigation disclosed no evidence of a psychogenic basis for the palsy.

As the classical features of familial periodic paralysis were recognizable in the history, attempts were made to induce symptoms. Four ounces (114 ml.) of glucose was given by mouth at 1 p.m. and again at 7 p.m. Weakness of the right arm and leg was reported the next day at 5 a.m., and of the left arm and leg at 6.15 a.m. By 10 a.m. all four limbs were in a state of flaccid paralysis with extinction of reflexes. Paralysis was profound on the right side, but weak movements of the left hand and foot indicated incomplete involvement of the distal muscles of the limbs on that side. Faradic reaction was abolished on the right side and feeble on the left. There was no motor disturbance of the trunk, neck, or head. The cranial nerves, abdominal reflexes, sphincter control, and sensory functions were normal. Urine was voided normally during the paralysis, but the bowel was not evacuated. Transient, mild glycosuria (0.02%), high acidity, and excess of urates were observed during the palsy. Results of systemic examination were otherwise negative. After a static period of about 26 hours, gradual return of power began distally and progressed to complete recovery in about 11 hours. Reflexes were restored later, but remained sluggish for about 18 hours, with coexistent aching and tenderness of the limbs. Four days later an attempt was made, without success, to provoke the palsy by subcutaneous injection of 10 min. (0.6 ml.) of adrenaline, repeated half-hourly from 9 a.m. to 3 p.m.

A spontaneous attack developed a week later, following exercise, the limbs of the right side only being affected. When paralysis was maximal 1 dr. (3.5 ml.) of potassium citrate in peppermint water was given by mouth. Symptoms passed off rapidly, with complete recovery in 3½ hours, leaving slight post-paralytic myalgia for about two hours.

As the patient's seizures were invariably nocturnal in incidence, a dose of ½ dr. (1.75 ml.) of potassium citrate was ordered as a routine prophylactic measure every night. No further recurrences were reported thereafter.

It was unfortunate that wartime conditions precluded biochemical study of this case—e.g., estimations of potassium, phosphorus, and sugar in the blood. I am not aware of a previous record of periodic paralysis affecting several members of an Indian family. The first such instance reported in a family in Britain is accredited to Farquhar Buzzard (1901). One of his three patients has recently described his symptoms, mentioning a persistent attack which had crippled him for three weeks (G. D. H., 1948).

I am grateful to Dr. C. Worster-Drought for his helpful comments and suggestions regarding this paper. He has kindly sent me an interesting note about one of three members of a family afflicted by this palsy who invariably develops attacks after bowling three or four overs at cricket, but never after batting or fielding. I am obliged to my colleague, Captain Oliver Medonza, for assistance in searching the literature available in Ceylon for references to this interesting syndrome.

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# Medical Memoranda

## Some Presenting Symptoms of Carcinoma of the Bronchus

Carcinoma of the bronchus may give rise to a variety of presenting symptoms due either to the primary growth or to secondary deposits. The table shows the mode of presentation in 17 cases seen during a six months' appointment as house-physician at the Essex County Hospital. In these unselected cases from the medical and surgical wards of a general hospital nearly half presented with symptoms caused by metastases.

*Presenting Symptoms*

| | *No. of Cases* |
|---|---|
| (i) *Caused by Primary Growth* | |
| Cough, haemoptysis, blood-stained sputum, pain in chest, dysphagia, superior vena caval obstruction | 9 |
| (ii) *Caused by Primary Growth but simulating Pleuro-Pulmonary Infection* .. | 2 |
| Fever and symptoms and signs suggestive of unresolved pneumonia or empyema. | |
| (iii) *Caused by Secondary Growth* | |
| Paraplegia .. .. .. .. .. | 3 |
| Cerebral tumour .. .. .. .. | 1 |
| Pain in abdomen (ileum) .. .. .. | 1 |
| Gross enlargement of liver .. .. | 1 |
| Total | 17 |

In cases in which carcinoma of the bronchus was diagnosed before secondary growth had caused symptoms death occurred within three months of the onset. Death supervened rapidly in this small series of cases, but some patients survive for two or three years after diagnosis. One case is worth recording in detail because of the unusual mode of presentation.

### CASE REPORT

Up to six weeks before admission this woman, aged 39, had been perfectly well. Her first complaint was of swelling of the face and upper part of the trunk. She also had some shortness of breath at that time, but no other symptoms.

On admission, on Sept. 9, 1947, her most distressing symptom was a massive, painful enlargement of both breasts. They were enormous and intensely tender; pitting oedema and peau d'orange was manifest. The right breast was larger than the left, and while she was sitting in bed this breast rested on her thigh. There was no discharge from the nipple; no localized inflammatory or other mass could be detected.

She also had a severe persistent cough, with brown blood-stained sputum. Her temperature was 104° F. (40° C.), pulse 200, and respiration rate 48. She was pale, cyanosed, very dyspnoeic, and obviously moribund. There was oedema and puffiness of her face and both upper limbs. The neck veins were engorged on the right side, but not on the left. Enlarged tender lymphatic glands were palpable in both axillae and in

the right supraclavicular region. Examination of the chest showed consolidation of the whole of the right lung and a pleural effusion. The liver was grossly enlarged and tender.

The diagnosis in this case was not easy. There was obviously superior vena caval obstruction, and carcinoma of the bronchus with large hilar secondaries seemed a likely diagnosis. The gross enlargement of the breasts developing so rapidly and the shortness of the history were both confusing factors. Her condition rapidly deteriorated, and she died three days after admission.

Post-mortem examination confirmed the diagnosis of carcinoma of the bronchus with lymphatic obstruction and obstruction of the superior vena cava. There was a purulent tracheitis, bronchitis, and there were multiple small abscesses containing thick yellow pus in the right lung, which was solid with grey pneumonic consolidation. The right bronchus led into a firm white mass at the hilum of the lung.

This growth invaded the right lung deeply and occupied a considerable part of the mediastinum, being about 6 in. (15 cm.) in diameter. In the mediastinum the mass was a mixture of primary growth and secondary glands. The growth had penetrated through into the right auricle and superior vena cava, which was partially occluded. The left lung was congested; the right pleura contained a large yellow effusion. There was a toxic change in the myocardium and gross "bread-and-butter" pericarditis with dilatation of the neck veins.

On sectioning the breasts, the enlargement was seen to be due to oedema, which was also present in the presternal subcutaneous tissue.

I am grateful to Dr. S. A. Propert, Honorary Physician, Essex County Hospital, Colchester, for permission to publish this case, and to Dr. J. B. Penfold, who performed the post-mortem examination, for his advice and criticism.

J. PETER BUSH, M.B., D.R.C.O.G.,
Obstetrician, North Devon Infirmary, Barnstaple.

## Pethidine as a Supplement to Nitrous Oxide Anaesthesia

The synthetic analgesic pethidine provides an alternative to morphine that possesses certain advantages over the natural alkaloid. The high degree of pain relief without respiratory depression or interference with the cough reflex, and the possession of certain atropine-like properties, have made it justly popular in obstetrics and in the relief of post-operative pain.

On a recent visit to San Francisco one of us saw this drug being administered intravenously as a supplement to nitrous oxide anaesthesia by Dr. William B. Neff, professor of anaesthetics at Stanford University, with excellent results both on the operating table and after. This use of pethidine does not seem to have been previously investigated in this country. We have since used it in upwards of 100 cases, with very gratifying results. It has been usual at the end of a long anaesthesia for the patient to reply to questions before leaving the table, and there has been a noticeable absence of post-operative pain and restlessness, often such a feature of other techniques where rapid recovery of consciousness occurs.

It has been our practice to put the patient to sleep with thiopentone and then administer nitrous oxide with some 30% of oxygen. An intravenous injection of 25 mg. of pethidine is given at the outset. This dose is repeated as often as is necessary to subdue any reflex activity on the part of the patient. We have found that 25 mg. of pethidine is needed about every 20–30 minutes in the average case. In abdominal and thoracic operations we have given occasional injections of "flaxedil" (a synthetic curarizing substance) or curare when the abdomen is tight or when the cough reflex is active. A rising pulse rate or blood pressure, or similar reaction to painful stimuli, is an indication that pethidine is required. The results during and after operation have been so good that we feel justified in publishing this early report, in case our colleagues may not be aware of the method.

We record our great debt to Dr. William B. Neff, who has developed this form of anaesthesia to a high degree.

WILLIAM W. MUSHIN, M.A., M.B., F.F.A. R.C.S., D.A.,
L. RENDELL-BAKER, M.B., D.A.,
Department of Anaesthetics, Cardiff.

## Splint to Control Dorsal Subluxation of Proximal Interphalangeal Joints of Fingers

In the *British Medical Journal* of Dec. 11, 1948 (p. 1030), Dr. Trevor Howell stated that the problem of deformed fingers with ulnar deviation and subluxation was unsolved. In many of these cases the main deformity is a dorsal subluxation of the proximal interphalangeal joint, and in the Cowley Road Hospital, Oxford, we have introduced a splint which controls the subluxation while allowing free flexion of the finger. The splint is constructed of a single piece of heavy-gaugé single-strand galvanized wire, padded and covered with leather. It consists of three transverse arms, one ventral to the proximal interphalangeal joint, and two others dorsal to the phalanges on either side of it. These arms are connected by side pieces, and the splint is so adjusted that the finger in maximum extension is slightly flexed, as in Fig. 1. As shown in Fig. 2, the splint forms

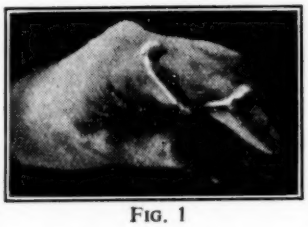

FIG. 1

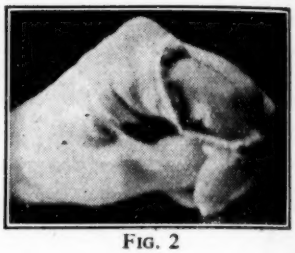

FIG. 2

no bar to flexion to the limit of the capacity of the joint. The side pieces of the splint should be tight enough on the finger to maintain the splint in position during flexion.

The patients who have been provided with these splints have remarked on an increased range of usefulness of the hand. This is because the finger can no longer "lock" in a subluxated position, and also because the initiation of flexion is carried out with the finger in a much more advantageous mechanical position for the flexors, and therefore with more power. Further, if fixation of the joint is progressing, it will occur in a more satisfactory functional position if the deformity is controlled. None of the splints have been worn long enough to show whether their use can be curative, but it is possible that it might be so after constant wear for a period of several months. The splint is also useful in cases of this deformity arising from other causes.

(Since this note was written one patient suffering from paralysis agitans has undergone a complete cure of this deformity and now has a good functional hand after wearing the splint for nine months.)

My thanks are due to Dr. J. H. Spence, medical officer to the Cowley Road Hospital, for permission to publish this account, and to Mr. Eric Hillsdon for constructing all the splints since production of the prototype.

JOHN L. INSLEY, B.M., B.Ch., D.L.O.

# Reviews

## ABDOMINAL SURGERY

*Abdominal Operations.* By Rodney Maingot, F.R.C.S. Second edition. (Pp. 1,274; 468 illustrations. £4 4s.) London: H. K. Lewis and Co. 1948.

In the second edition of his book Mr. Maingot tells us that the considerable advances made in abdominal surgery during the last few years have forced him to revise the whole work thoroughly in order to bring it up to date. This revision is at once apparent, for the original two-volume book published in 1941 now consists of a single volume; and whereas the first edition was Mr. Maingot's own work throughout, with the exception of two chapters by two contributors who no longer appear, the present is the handiwork of eight new contributors in addition to the original author. The modernity of the book may be gathered from the fact that Chapter 16, by Lester Dragstedt, is on section of the vagi in the treatment of peptic ulcer. Certain omissions commented upon in reviews of the first edition have been made good; thus, there is an index of authors as well as of subjects. There is also a chapter by A. J. Cokkinis in which malrotation of the gut is discussed. In this section more reference might have been made to Norman Dott's notable paper on the subject. The historical notes which appear in various parts of the book, such as those in the chapters on subphrenic abscess, appendicitis, and diverticulitis, are excellent, many of them containing quotations from original papers.

In the diagram of various modifications of the Billroth II type of gastric resection (p. 223) I should like to have seen the Moynihan II no-loop, isoperistaltic anastomosis shown, as this has proved highly successful in the hands of many of his disciples and appears to be still popular. There are a few errors in the spelling of proper names—the appearance of Sir William's name as MacEwan (p. 820) may cause distress in Scotland, and that of Rodgers (p. 108) without the third letter lead to discontent in Northern Ireland.

There is an excellent chapter by Mr. R. C. Brock on post-operative chest complications and their management, but except for an article on local analgesia there is still no section on anaesthesia, an omission which was also commented upon in the review of the first edition. Perhaps the distinguished author prefers to leave the selection and administration of anaesthetics entirely to the anaesthetist, but the safety and ease of performance of abdominal surgery and the incidence of post-operative complications are so closely linked with the nature of the anaesthetic and its method of administration that a place might be found for general guidance in these matters in order to make this book complete.

This is a masterly work, the text of which is well arranged, clear, and eminently readable, while the illustrations are outstanding. Special notice should be given to them, since their importance in such a book, which is to be a guide to operating surgeons, cannot be overstated. They are for the most part the work of the Misses Larivière and McLarty and represent fine craftsmanship of which British surgical publishing may well be proud. The figures are clear and accurate as well as realistic, and should be a decided help to the young surgeon in the process of developing his technique or seeking guidance about an operation with which he is not very familiar. Some pathological material is well shown in both coloured and black-and-white plates by well-known medical illustrators such as Thornton Shiells, A. K. Maxwell, and others.

Among a series of textbooks on abdominal surgery Moynihan's two-volume book was outstanding up to the time of his death and for some years later. This is a work which in many respects resembles it, and bids fair to be a worthy successor and as valuable a guide to this generation as that of the great Leeds surgeon was to the generation before it. The author appears to have fully achieved his purpose of presenting a detailed consideration of the technique of modern abdominal operations.

LAMBERT ROGERS.

## SURGERY OF THE STOMACH

*The Surgery of the Stomach and Duodenum.* By T. H. Somervell, M.A., M.B., B.Ch., F.R.C.S. (Pp. 546; illustrated. £2 5s.) London: Edward Arnold and Company.

Mr. T. H. Somervell, whose advocacy of "physiological gastrectomy" is well known, has here collected the results of his exceptionally wide experience of the whole range of gastric surgery. Although he is a complete convert to Hey's operation of vasoligation with, or occasionally without, an associated gastro-jejunostomy, his book is as unbiased an account of the surgical attack upon peptic ulceration as one could wish for; indeed, the description of his favourite method of treatment occupies but eleven pages of the book's total of over 500. His conclusions on this subject are well summed up in the preface: "It is not everyone who can perform an adequate gastrectomy with a low enough mortality to make it a justifiable operation. But many surgeons can do vagotomy, and all surgeons worthy of the name can devascularize the stomach with negligible mortality. All the evidence we have so far collected goes to show that the results of this operation are good." The chapter on vagotomy is written by Mr. Orr, who gives a well-balanced account of this innovation, including descriptions of both the transthoracic and the abdominal supradiaphragmatic operations.

The general outlook of the book is essentially balanced, and in controversial matters the author has been at great pains to present both sides of the question quite fairly; nevertheless, he usually has a definite opinion of his own. For instance, he is not in favour of the non-operative or expectant treatment of perforation except in the very gravest type of bad-risk patient, but he favours the Fowler position after operation provided all air is expelled from the peritoneum. He thinks that in very special circumstances there is a place for gastrectomy in the treatment of perforation. On the debatable question of the surgical treatment of bleeding from ulcers he is less definite, believing that the correct answer depends upon the capabilities of the individual surgeon: "For patients who are in the hands of an experienced surgeon I am in favour of early operation within 24 hours of the bleeding, backed by a transfusion controlled by intelligent observation." But how the surgeon is to assess his own capabilities cannot be told. He is enthusiastic on the transdiaphragmatic and transthoracic routes for access to the cardiac end of the stomach or oesophagus, and gives a good description of these operations. These are a few examples of the valuable conclusions and teaching to be found in these pages.

The book is well and copiously illustrated, the reproduction of radiographs and photomicrographs on the semi-art paper being particularly good. To sum up, this is a volume which can be highly recommended both to the novice and to the more experienced, for it is written modestly and with obvious sincerity.

NORMAN C. LAKE.

## RADIOLOGY OF THE GUT

*The Digestive Tract in Roentgenology.* By Jacob Buckstein, M.D. (Pp. 889; 1,030 illustrations in 659 figures. £5.) Philadelphia and London: J. B. Lippincott Company.

The author's twenty-five years' association with Bellevue Hospital, New York, as a visiting radiologist, have provided him with a wealth of experience in gastro-enterological radiology.

The material presented in this book has been carefully and systematically selected. Each section is prefaced by a short anatomical description, a historical sketch, and a well-illustrated account of the normal appearances of the part under discussion. The method of examination of the part is described briefly in each major section. A short history of any case described is followed by the clinical, operative, pathological, and radiological findings. The radiological opinion is reserved to the end of the presentation. There is no air of infallibility, and where errors were made in the diagnosis the reasons are given without reserve.

Over a thousand illustrations of very fine quality are used, and they are properly keyed to the text so that the reader can follow them with the minimum of page turning. They really do show the points made, which is not true of all books on radiology. Each section has a satisfactory bibliography which is selected from publications in many languages.

Some of the author's statements are open to challenge. Many would not agree with him that "gastritis is a comparatively frequent disease," but they would share his caution in making the diagnosis radiologically. There is no doubt also that air in the duodenal cap is derived from that in the stomach, though the author would only presume so. In the discussion of short oesophagus the condition is considered solely as a congenital abnormality, and the possibility that shortening may occur later as a result of ulceration is not mentioned, even though a case fully described would seem to fit into the acquired category.

These are minor criticisms, and the book is strongly recommended in spite of its heavy cost: it provides a ready source of reference for the experienced radiologist and clinician, as well as being an excellent textbook for the junior radiologist or postgraduate trainee. The printing and paper are good and the bibliographic and general indices are clearly drawn up.

F. PYGOTT.

## A SCHEME OF NEUROLOGY

*A Textbook of Clinical Neurology.* By J. M. Nielsen, M.D. Second edition. (Pp. 699. $7.50.) New York: Paul B. Hoeber, Inc.

Dr. Nielsen says in his preface to the first edition, "The book aims to present the subject of clinical neurology working from the simple to the complex . . . in so concise and clear-cut a manner and in sufficiently small volume that it may be used as a text of the subject during the time allotted to neurology in a general medical course." To this end he has systematically described the pathology and effects of diseases of each part of the nervous system, beginning at the periphery and finally reaching the hemispheres. He has then considered different forms of disease in turn; there are chapters on inflammations, tumours, and trauma, for example, and he has described entities such as the epilepsies, migraine, and intellectual defect in separate sections. Finally, he has an account of such special subjects as electro-encephalography, diseases of bones, and the vitamins. There are also two articles on neuroses and addiction which, though short, are much more useful than in comparable textbooks of neurology.

The presentation of neurology in this book follows the German method, with an emphasis on syndromes and proper names which is now unfamiliar in this country, and which many think undesirable. This is most clearly shown in the chapter on syndromes of the brain stem, which includes not only the Wallenberg syndrome, the Millard–Grubler syndrome, and the Fovilles syndrome, but also Avellis's, Schmidt's, Jackson's, and many others. This form of presentation makes a demand upon memory which is beyond the capacity of some students and most neurologists.

The second edition has been brought up to date, particularly the sections on the treatment of infections. It is admirably produced and well illustrated.

DENIS WILLIAMS.

## THE BASIS OF DISEASE

*Biology of Disease.* By Eli Moschcowitz, M.D. (Pp. 221. $4.50.) New York: Grune and Stratton. 1948.

In this collection of 24 essays, previously published in various journals, the author is concerned with the biological processes underlying a variety of clinical syndromes. He feels that too detailed classification of diseases is potentially dangerous, because thereby we may obscure the fact that similar derangements of function are common to several of them. Moreover, he believes that a number of chronic diseases are not separate entities, but represent the same morbid process at different stages of evolution. Thus he regards neuro-circulatory asthenia as the precursor state of Graves's disease, and cites examples where he has had patients under prolonged observation and has watched the transition.

The author displays an eclectic taste in his range of subjects. He discusses on the one hand common conditions such as arteriosclerosis, peptic ulcer, uraemia, Graves's disease, and obesity, and on the other uncommon illnesses such as periarteritis nodosa, Libman–Sachs disease, and follicular lymphoblastoma. Because of his preoccupation with the dynamics of disease rather than with the accompanying diverse morphological changes, however, he achieves unity—which is all the more surprising because the book appears at first sight to be a conglomeration of articles on unrelated subjects.

Dr. Moschcowitz writes with enthusiasm about psychosomatic medicine. As he points out, it is as old as Hippocrates in conception, but recent years have been fruitful in clarifying our understanding of this aspect of disease. Among psychosomatic disorders he defines a group of hyperkinetic diseases which includes essential hypertension, Graves's disease, peptic ulcer, and cardiospasm, in all of which he believes there is a primary exaggeration of function followed by marked anatomical changes. He observes five stages in their evolution: (1) the constitutional, (2) the exaggeration of function, (3) the lability of signs and symptoms, (4) the fixation of this exaggerated function, (5) somatic changes. Unfortunately he does not throw new light on why emotional stress has different effects on different people. He recognizes this important gap in our knowledge, and, though rejecting the Adlerian postulate of "organ inferiority," can only fall back on the all-embracing concept of "constitution" as an explanation.

Not all of us will agree with his opinions, but most of us will enjoy reading his book.

SIDNEY TRUELOVE.

## REFLECTIONS ON GENERAL PRACTICE

*Cum Notitia: Reminiscences of a General Medical Practitioner.* By D. A. Alexander, M.B., Ch.B. (Pp. 395. 12s. 6d.) Bristol: John Wright and Sons. 1949.

An unusual book which left me sorry that no more information is given about the author than can be gathered from the text and the scanty note in the foreword. This introduction merely tells us that it is a collection of medical papers arranged as letters from a father who loved his profession to a son who felt unable to follow it, and that the author died suddenly before the book could be published. It is clear, however, that he was a happy man of wide reading and culture who was intensely interested in his patients. He was old-fashioned in some ways, but curious about new developments which might help him in his work and answer some of the questions about which he was always speculating. He tells us that an editor to whom he submitted a paper said, "You are a born speculator"—a verdict which all readers of this book will endorse.

It is a discursive work. The bulk of it is taken up by many careful and picturesque case histories. There are occasional, and too rare, reminiscences of colleagues and assistants, and a vivid account of his visit to the B.M.A. Annual Meeting at Cambridge in 1920. He had been anxious to meet Sir Clifford Allbutt, for whom he had great reverence, and like most of us who were present was disappointed with Sir Clifford's portrait that was presented to him at the meeting. "In it," he says, "I could not see all that we admired in the Regius Professor." I liked his defence of routine and mechanical work (p. 256).

I hope I have given the impression that this is a book to be dipped into and savoured. It is a worthy record of some aspects of an obviously good man who was a general practitioner far above the average.

ALFRED COX.

## MARRIAGE GUIDANCE

*Marriage Counselling.* By David R. Mace, M.A., B.Sc., Ph.D. With foreword by the Right Hon. Henry Willink, *M.C.*, K.C. (Pp. 167. 8s.) London: J. and A. Churchill. 1948.

The reader of this excellent book need no longer complain he does not know what marriage guidance is or what it tries

to do. Dr. Mace sets out in clear and simple language all that an inquirer seeks to know.

The backbone of marriage guidance is the group of counsellors at the centres throughout the country, who work for the most part on a voluntary basis. These counsellors correspond to general practitioners in medicine, and their function is to sort out the cases, arrive at a diagnosis, and where necessary refer them to specialists (who may be medical, psychological, social, spiritual, or legal). Reference to medical specialists should be through the patients' own doctors. The success of marriage guidance depends on team work, since the causes of unsuccessful marriage are manifold; each case presents an individual problem, and no one counsellor can expect to be able to cope with all.

The work should comprise education for marriage, suitable for all young people over 16, preparation for marriage for engaged couples, and guidance and remedial treatment for those already married. In the past too much of the work has been with desperate cases where the situation has almost or quite passed beyond control. Even so, some measure of success has been achieved, though accurate statistical evidence cannot be obtained. It is hoped that in the future more preventive work may be possible as the public gains confidence in the efficacy of the centres. The help given must be competent, sympathetic, and confidential, and the counsellors must be most carefully selected. The methods used for selection are described. On the whole, married middle-aged people are the best, as they are most acceptable to both husband and wife, who must almost invariably be interviewed separately. The counsellors work for sessions of three hours not more than once a day, often only once a week. The general aims are emotional catharsis, elucidation and explanation, and mediation. With increasing experience less and less recourse to specialists is necessary.

While trying to keep an open and uncritical mind on all problems, there are certain ethical principles which are maintained. Extra-marital intercourse is condemned; contraceptives are permitted and in some cases encouraged. No decision about artificial insemination has yet been reached. Although every effort is made to seek a solution other than divorce, in some cases it is regretfully admitted to be unavoidable. No attempt is made to quote individual cases, but there is a general survey of the causes of marital disharmony.

There is no doubt that marriage guidance has come to stay; it now has Government support as a constructive effort to allay the social menace of the broken home with all its attendant evils, and this book should have a wide circulation in order that the public, who ought to be interested, may learn what it is all about.

R. G. GORDON.

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Percival Bailey's *Intracranial Tumors* (second edition; pp. 478, 155 figures, 16 plates; $10.50 or £2 15s.; Springfield, Illinois: Charles C. Thomas; Oxford: Blackwell Scientific Publications, 1948) has been out of print too long, for it is a useful book of an unusual kind. It is written in an authoritative fashion by a man who knows very clearly what he thinks about the brain, its structure, its functions, and the nature and effect of the tumours that grow in it. It is essentially an American book showing little, except inferentially, of British influence on neurology and neurosurgery. The basic plan of the work is pathology, a good starting place and one that befits the author, whose part in the identification and classification of brain tumours is well known. The clinical effects of tumours in various situations are demonstrated by graphic descriptions, often transcripts of what patient and doctor said to one another. The only disadvantage of this is that tumours in the same situation do not produce stereotyped results, so that the inexperienced clinician who expects his patients to make the interesting replies that Dr. Bailey records may fail to recognize the site of the lesion in someone else. This is particularly true of frontal tumours, the typical effects of which are not only frequently absent but may be mimicked by tumours elsewhere. The book is well and plentifully illustrated; the diagrams are good, though some of the more ambitious pictures are not. But, even though it has faults, Dr. Bailey's book retains its place as highly important. It is a statement of his own views, an account of his thoughts on a subject to which he has made many contributions of the greatest interest and importance.

## BOOKS RECEIVED

[*Review is not precluded by notice here of books recently received*]

***Operative Technic in General Surgery.*** Edited by W. H. Cole, M.D., F.A.C.S. (Pp. 951. No price.) New York: Appleton-Century-Crofts. 1949.

***Tumors of Bone.*** By C. F. Geschickter, M.D., and M. M. Copeland, M.D. 3rd ed. (Pp. 810. 105s.) London: J. B. Lippincott. 1949.

***Cunningham's Manual of Practical Anatomy.*** Edited by J. C. Brash, M.D., F.R.C.S.Ed. 11th ed. (Pp. 488. 21s.) London: Geoffrey Cumberlege. 1948.

***A Textbook of Practical Nursing.*** By K. O. Brownell, R.N., B.S. 3rd ed. (Pp. 465. 19s.) London: W. B. Saunders. 1949.

***Trends in Nursing History.*** By E. M. Jamieson, B.A., R.N., and M. F. Sewall, B.S., R.N. 3rd ed. (Pp. 632. 22s. 6d.) London: W. B. Saunders. 1949.

***Training for Childbirth.*** By M. Randell, S.R.N., S.C.M., T.M.M.G., F.C.S.P.(Hon.). 4th ed. (Pp. 142. 10s. 6d.) London: J. and A. Churchill. 1949

***Cardiac Catheterization in Congenital Heart Disease.*** By A. Cournand, M.D., and others. (Pp. 108. 22s.) London: Geoffrey Cumberlege; New York: The Commonwealth Fund. 1949.

***Atlas of Roentgenographic Positions.*** By V. Merrill. Vols. 1 and 2. (Pp. 663. 150s.) London: Henry Kimpton. 1949.

***Outline of the Amino Acids and Proteins.*** Edited by M. Sahyun, M.A., Ph.D. 2nd ed. (Pp. 286. 30s.) London: Chapman and Hall. 1948.

***Progress in Allergy.*** Edited by P. Kallos. Vol. 2. (Pp. 356. 36 Swiss francs.) New York and Basle: S. Karger. 1949.

***Cancer of the Uterine Cervix.*** By F. Truelsen. (Pp. 440. No price.) London: H. K. Lewis. 1949.

***Studies on Hookworm Disease in Szechwan Province, West China.*** By K. Chang. (Pp. 152. $3.) Baltimore: The Johns Hopkins Press. 1949.

***Die Tuberkulose des Kindes.*** By H. Brügger and others. (Pp. 340. M. 16.) Stuttgart: Georg Thieme. 1948.

***Medizinische Klinik.*** By F. Hoff. (Pp. 467. M. 29.60.) Stuttgart: Georg Thieme. 1948.

***Semiologia y Patologia de la Articulacion de la Rodilla.*** By J. A. Pique and C. Khoury. (Pp. 185. No price.) Buenos Aires: Lopez and Etchegoyen. 1948.

***Lehrbuch der Inneren Medizin.*** By T. Brugsch. Vol. 2. (Pp. 818. M. 30.) Berlin: Urban and Schwarzenberg. 1948.

***Physiologie du Système Nerveux Central.*** By G. Morin. (Pp. 267. 950 francs.) Paris: Masson. 1948.

***Medizin in Bewegung.*** By R. Siebeck. (Pp. 520. M. 27.) Stuttgart: Georg Thieme. 1949.

***Tos Ferina.*** By J. P. Diaz. (Pp. 294. No price.) Saragossa: Revista Española de Pediatria. 1949.

***I Reticolociti.*** By M. Ninni. (Pp. 296. No price.) Pavia: Tipografia del Libro. 1949.

***Streptomycin und die Behandlung Haematogener Tuberkuloseformen.*** By O. Ruziczka. (Pp 179. 24s.) Vienna: Springer. 1949.

***L'Ultra-Violet, la Lumière Solaire et Artificielle, l'Infra-Rouge.*** By J. Aimard and H. Dausset. 7th ed. (Pp. 231. 800 francs.) France: L'Expansion Scientifique Française. 1949.

***Lehrbuch der Massage und Manuellen Gymnastik.*** By W. Thomsen. 2nd ed. (Pp. 237. M. 16.50.) Stuttgart: Georg Thieme. 1949.

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## THE LAST OF THE GREAT EUROPEANS

Men of science have often been prominent among the great amateurs of the arts. But it is now unusual for poets, painters, or musicians to be serious students of science. In this issue of the *Journal* we are privileged to publish an appreciation of Goethe, whose bicentenary is now being celebrated, from the pen of Sir Charles Sherrington. It is surely fitting that the doyen of British scientists, whose profound knowledge of European literature illuminates the whole of his paper, should pay tribute to a great poet who not only studied science seriously but contributed original observations of his own. Goethe's influence on scientific thought is no longer widespread, but regard for his genius among "a cultivated public our civilized world over" still remains as great as ever.

The German word *Heiterkeit* is untranslatable. Perhaps "cheerful serenity" is as close a rendering as we can contrive in English. Goethe was one of the few great men of the modern age who had a deep sense of tragedy and yet achieved *Heiterkeit*. It was by no means his constant mood, for he was one of the moodiest of men. He was also a man of strong passions. His moods would chase one another with extreme rapidity. His passions were deep-seated and endured until the end—he was 83 when he died. His mind combined to an extraordinary degree the perceptive and creative faculties. Even in the year of his death he was so full of ideas and projects that he felt as though all the world were still before him. Goethe's was a complete and perfectly integrated personality—integrated both in itself and with external Nature, or what we have come to regard as that, for to Goethe, as to the ancient Greeks, Nature was not external. Nature to him was everything. It was for this reason above all that he could not accept Christianity; the doctrine of the Fall, the rupture in Nature, and the ineradicable sinfulness of man were wholly alien to his spirit. He could not accept the mediaeval view as expressed by Chaucer in the line:

> Nature, the vicaire of th' almyghty lorde.

For Goethe, God and Nature were one—complete and perfect. There would be something gruesome in his poem on the skull of his friend Schiller as it lay in the charnel-house, some inappropriate recollection of Hamlet musing over the skull of Yorick, were it not for the grandiose conception which makes the skull the temple of genius (an ancient temple, as it were, that once housed a divine spirit) and for Goethe's deep awareness that the skull is itself a noble structure and organic form. The poem, one of Goethe's greatest, ends with the marvellous—but untranslatable—lines:

> Was kann ein Mensch im Leben mehr gewinnen,
> Als dass sich Gott-Natur ihm offenbare?

All the emphasis lies upon *Gott-Natur*—God-Nature—the organic principle, the essence of all that Goethe believed in, lived and worked for, his religion and his philosophy in one. For theology he cared little, and for systematic philosophy even less, though he deeply revered Spinoza. That God-Nature should reveal itself to a man as it did to Schiller—this is the greatest happiness in life, the only enduring gain, the only fulfilment. Such is the meaning of these two lines which only a great poet could transmute into another language.

Goethe was a man who suffered much, and his "cheerful serenity" was but the aspect—though the inner as well as the outer aspect—of anguish and passion mastered and yet not forgotten. What was most astonishing about him was the immense power of intellect and imagination which enabled him to harmonize all contraries and discords in himself, in history, and in the world of his day. Although one of the deepest of writers, he was one of the least paradoxical. His conception of classical antiquity is out of date from an archaeological point of view, for modern research has disclosed what might be called the ancient underworld—the dark and daemonic forces in Greek religion, and the pessimism of the Greeks to which the great Burckhardt first called attention. Goethe saw "cheerful serenity" above all in the Greeks. And surely it is there; but much is there also of which Goethe had no knowledge. His judgment of Greek sculpture, known to him almost entirely through inferior examples of the late decline, is not our judgment. But even when he was mistaken he was profound and illuminating. We cannot simply discard his perception of classical antiquity. That perception did not merely record certain data—Goethe was little interested in data. Nor was it an *apparatus criticus*. It was a way of looking at things in their totality.

Although, as Sir Charles Sherrington points out, most of Goethe's work as a scientist has been superseded, it has extraordinary merits. Even when it is entirely mistaken it is interesting—and always readable. His work on the nature of colour has a value which made Turner, the greatest of English colourists, treasure it all his life. Goethe as a scientist did not seek for proofs, but propounded organic conceptions. He had an extraordinary sense of significant form.

Goethe despised politics, and yet few writings are as replete with political wisdom as his. The Germans were not yet a nation in his day. He warned them against trying to become a nation, and he told them: Do not on any account try to imitate Napoleon. The French Revolution was repugnant to him, but he had the gift of observing political phenomena *sine ira et studio* and yet with deep understanding, just as he would observe natural phenomena. He admitted that the French Revolution produced a revolution in himself, but the harmony of his own nature prevailed. He hated presumptuous ignorance. "There is nothing," he said, "more terrible than ignorance in action."

Classical antiquity, the Renaissance, and the modern world came together in Goethe. This is evident, above all, in his supreme masterpiece, the second part of *Faust*. Every character in this gigantic architectural poem is a type, every scene is symbolical, every event is significant. The poem contains the most grandiose scene of classical beauty in modern literature—the *klassische Walpurgisnacht*. It has the audacity and the sensuous splendour of the Renaissance and the perplexity, the sense of crisis, that mark our own time. He finished this work just before he died, fully aware that it would not be understood by his contemporaries. Only in our own generation has understanding come.

The period that immediately followed Goethe's was a period of prophetic genius—of Kierkegaard, Dostoevski, and Nietzsche. These great men were Europeans too, though Dostoevski would have disclaimed that title, but they belonged to the Europe that was already breaking apart. They not only stood on the verge of the abyss: they were already of the abyss. Goethe saw the abyss, but he was never of it. He was a prophet, but prophecy was not his vocation. His vocation was not to warn but to fulfil, not to paint the future or recall the past but to contemplate and reveal in symbolical terms—through the medium of poetry, drama, fiction, and science—the living, organic whole which, while it is always changing, is always the same. He would have rejected the evolutionary hypothesis, for to him Nature was complete and perfect, and every change was but a change from one perfection to another. He was a great moralist. He regarded evil as something against Nature, because Nature was not the realm of free and arbitrary impulse but the realm of form, structure, harmony, and law.

His genius was the last embodiment of that organic unity which the modern world has lost. He was the last of the great Europeans. The relevance of his warnings grows with every year. His influence upon his own generation and those that followed was pervasive—a kind of creative radiation, not an impact. He formulated no doctrine that moved the masses. Not one of his ideas stands alone. All his ideas—and they were many and varied—belong organically to one living conception. That the bicentenary of his birth should be celebrated throughout Europe and wherever European civilization has spread is evidence that Europe is not lost.

## AN ANTIBIOTIC OF WIDE RANGE

We have referred on several recent occasions to reports from the U.S.A. on the therapeutic properties of "aureomycin."[1] Earlier accounts of this new antibiotic were not encouraging: indeed, its properties as demonstrable *in vitro* are such that an entire absence of therapeutic effect would not have been surprising. It is exceedingly unstable in ordinary culture media, so much so that the method of assay recommended is one in which the results can be read after only four hours' incubation. It is much less active in neutral or alkaline than in acid media, and serum diminishes its activity. That these unpromising characters are for some reason quite unrepresentative of the behaviour of aureomycin in the body is clear from the growing volume of clinical reports on its efficacy in a wide variety of infections. It has in fact a greater range of therapeutic activity than any other antibiotic, and its popularity in the U.S.A., where it is now being used on an enormous scale, is much enhanced by the ease of its administration. It is taken by mouth, and, although sometimes producing nausea, vomiting, and diarrhoea, is apparently free from any risk of more serious toxic effects.

With its action in rickettsial infections we in this country are fortunately not directly concerned, but the fact that there is now an effective treatment for typhus and similar diseases is a therapeutic advance of the first importance: in this the honours are shared between aureomycin and chloramphenicol ("chloromycetin"). Aureomycin has also an action on several viruses, including those of lymphogranuloma venereum and of primary atypical pneumonia. The latter disease was the subject of a very careful study by Meiklejohn and Shragg,[2] who laid down strict criteria in selecting their patients, whose disease was of rather more than ordinary severity. They also treated an exactly comparable control group with penicillin. Although about half the control group recovered fairly rapidly, a prompt therapeutic response was invariable in those treated with aureomycin. A few patients relapsed, but they responded rapidly to further treatment. It is a remarkable fact that aureomycin is a specific for every common form of

[1] *British Medical Journal*, 1948, **2**, 1112, and 1949, **1**, 763, and **2**, 431.
[2] *J. Amer. med. Ass.*, 1949, **140**, 391.
[3] *British Medical Journal*, 1949, **2**, 257.
[4] *Proc. Mayo Clin.*, 1949, **24**, 302.
[5] Ibid., 1948, **23**, 569.
[6] *J. Amer. med. Ass.*, 1948, **138**, 1145.
[7] *Lancet*, 1949, **2**, 326.
[8] *British Medical Journal*, 1949, **1**, 1037.
[9] *Ann. N.Y. Acad. Sci.*, 1948, **51**, 267.
[10] *Proc. Mayo Clin.*, 1949, **24**, 309.

pneumonia, whether due to a bacterium or a virus. Among highly susceptible bacteria are the pneumococcus and other Gram-positive cocci, and *H. influenzae* and certain other Gram-negative bacilli: susceptible viruses are those of primary atypical pneumonia and of psittacosis. It is perhaps unnecessary to point out that the demand for a drug which can justifiably be given on making the clinical diagnosis of pneumonia, without waiting for, or even undertaking, a bacteriological diagnosis, is likely to be considerable.

To pneumonia in general can be added venereal disease in general, as was pointed out recently in this *Journal* by Drs. R. R. Willcox and G. M. Findlay.[3] Lymphogranuloma venereum and granuloma inguinale have both been found to respond, as also have syphilis, gonorrhoea, and, in the experience of the authors quoted, non-specific urethritis associated with the presence of pleuropneumonia-like organisms. It should be understood that the action of aureomycin on gonorrhoea is inferior to that of penicillin, and only likely to be exploited should penicillin-resistant strains of gonococci appear, and that its effects in syphilis require much further study. Information about the latter is confined to a few reports from the Mayo Clinic, in the latest of which O'Leary and his colleagues[4] describe the rapid healing of lesions of late cutaneous syphilis, and the early stages of a study of the treatment of neurosyphilis. It should be remembered that Heilman[5] has already shown experimentally that aureomycin is more effective weight for weight than penicillin in the treatment of relapsing fever and leptospirosis: thus evidence of activity against "spirochaetes" is accumulating.

Aureomycin is now acknowledged to be much inferior to chloramphenicol for the treatment of salmonella infections, including typhoid fever. On the other hand, the evidence is now conclusive that it has a remarkable effect in brucellosis. Spink and his colleagues[6] are among those who have gone to Mexico to exploit the abundance of clinical material of this kind to be found there, and they report enthusiastically on the treatment of 24 patients with bacteriologically proved *Br. melitensis* infections, some being of great severity. Debono[7] also has reported from Malta that the immediate response to treatment was excellent in 24 patients infected with *Br. melitensis*. The successful treatment of a patient with a *Br. abortus* infection was described recently in this *Journal* by Galpine.[8] Among other bacterial infections, nothing conclusive about the action of aureomycin in tuberculosis has yet been reported, though a single observation by Schoenbach and his colleagues[9] suggests that there is such an action. On the other hand, it is already quite clear that a wide field of essential use for aureomycin exists among penicillin-resistant infections due to staphylococci. The increasing prevalence of these organisms has caused much disquiet, and is amply confirmed by Nichols and Needham,[10] of the Mayo Clinic, who found that of 50 recently isolated strains 34 were resistant to penicillin and 14 to streptomycin, but all were sensitive to aureomycin. In the last 15 cases of staphylococcal bacteriaemia treated at the Mayo Clinic the organisms from 12 were penicillin-resistant and from three streptomycin-resistant: all were inhibited by 0.78 μg. per ml. of aureomycin. Six of these patients were actually treated with aureomycin, with successful results in four.

There are so far few references in the American literature to the use of aureomycin in this type of case, but it is now a common practice, and aureomycin rather than streptomycin is generally regarded as the second line of defence when penicillin fails against staphylococci. Indeed, some authorities even go so far as to say that aureomycin should be given in addition to penicillin from the outset in a severe case, pending determination of the penicillin sensitivity of the organism. It remains to be added that, since aureomycin is active against all organisms commonly causing urinary tract infections except *Proteus* and *Ps. pyocyanea*, it is now very widely used in the U.S.A. as a urinary antiseptic, sometimes even before other drugs have been tried. Some of these uses are non-essential, and others, notably the treatment of rickettsial infections, do not concern us in Great Britain. But there remain three diseases in which aureomycin may sometimes be the only means of saving life. The task of those who have to decide how many precious dollars to spend on this new antibiotic and how to distribute such supplies as reach this country can be no easy one.

## STREPTOMYCIN IN INFANTILE GASTRO-ENTERITIS

The rational use of chemotherapeutic drugs in infective gastro-enteritis of infants is made difficult by the many varieties of organisms to which aetiological significance has been attributed. A careful bacteriological investigation by Taylor, Powell, and Wright[1] was published in a recent issue of this *Journal*. The wide range of action of streptomycin, especially against Gram-negative bacteria, made it an obvious choice for clinical trial in this disease. Preliminary results indicate that even when no pathogenic organisms are isolated from the stools streptomycin may be effective, and among the earlier reports those of Leisti,[2] who treated 46 infants, all with negative stool cultures, and of James and his colleagues,[3] who isolated *Proteus vulgaris* from most of their cases, are favourable. The latter authors found that oral streptomycin alone was effective whether or not other foci of infection were present, and that even critically ill children were ready for discharge from hospital in from 9 to 12 days. However,

[1] *British Medical Journal*, 1949, **2**, 117. See also leading article, p. 141.
[2] *Ann. Med. intern. fenn.*, 1947, **36**, 575.
[3] *Lancet*, 1948, **2**, 555.

the conclusions of Drs. A. Holzel, G. Martyn, and L. Apter and of R. Debré and P. Mozziconacci in the papers published elsewhere in this issue show that much has yet to be learned.

The former conclude that streptomycin had no specific effect in cases which they studied. Seventy-nine infants were divided into three groups: the first, consisting of 26 cases, was given oral streptomycin; the second (24 cases) received intramuscular streptomycin; and the control group of 29 cases was not given chemotherapeutic treatment. The numbers of deaths in the three groups were 5, 6, and 3 respectively. The presence or absence of parenteral infection made no difference to the outcome. In 63% of the cases a type of *Bact. coli* var. *neapolitanum* was isolated from the faeces, but the authors do not consider that their findings indicate that this organism was necessarily the cause of the infection. The failure of streptomycin treatment in some cases may be attributed either to development of resistance by this organism or to cross-infection with a resistant strain. Although great improvement occurred in some infants, in others the drug had no effect, and the indications for antibiotic therapy in this condition remain obscure.

In the series of 41 cases of septicaemia and meningitis in infants reported by Debré and Mozziconacci the infection was due to intestinal organisms—members of the *Bact. coli* and *Salmonella* groups, *Ps. pyocyanea*, or other Gram-positive organisms. Signs of gastro-enteritis were an important clinical feature in all these cases. Streptomycin was administered intramuscularly and, where appropriate, by the intrathecal or intraventricular routes. Some of the patients received sulphonamide in addition. Twelve out of 16 cases of septicaemia without meningitis recovered, but only four recovered out of 25 cases in which meningitis was a complication. Again, many of the failures might be attributed to resistance of the organism. Strains obtained from blood or cerebrospinal fluid were sometimes sensitive to between 150 and 200 μg. per millilitre—concentrations which are not usually attainable clinically—but the authors were unable to find any relation between resistance and clinical progress, and they emphasize the importance of lesions which interfere with the diffusion of the antibiotic. Evidently the recovery of a streptomycin-sensitive organism from a case of infantile gastro-enteritis is not a reliable indication for streptomycin therapy. There are other, as yet unknown, factors which are important, and until these are elucidated treatment must remain largely empirical.

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## MEDICAL PROBLEMS IN WESTERN GERMANY

The medical problems of Western Germany are those of the whole of Western Europe writ large but with some special distinguishing features. A great increase in the population followed the exodus from Eastern Europe, and many doctors are among those who have had to leave their homes; some of these are still in displaced-person camps. Medical posts have yet to be found for doctors who were in the Services, or who have returned from prisoner-of-war camps in Russia, or who have fled from intolerable political conditions. Inevitably in a period of readjustment such as the present there are occasional complaints, mostly, it would seem, unfounded, that appointments have been made less on professional than on political grounds. All the medical schools are overcrowded with students and young doctors: a professor of medicine, for instance, will have at least a dozen paid assistants, in addition to a number of voluntary workers. Bomb damage has reduced the numbers of hospital beds, which would in any case have been insufficient to meet the needs of the increased population. In the now disused S.S. barracks, however, space has been found for additional hospitals, and many of these grim buildings have been skilfully converted into hospitals with self-contained cubicles for the nursing of patients with infectious diseases. Outside in the corridors are still the racks for stacking rifles. The bomb-proof underground bunkers constructed in many hospitals are still in use, in some cases as neurosurgical clinics where patients with brain lesions can be given complete quiet and rest. Bed linen at first was scarce, but now, after the devaluation of the mark in June, 1948, everything has become more plentiful. Penicillin is at last being produced on a commercial scale. Streptomycin too is available, and in one children's clinic it was claimed that 36 out of 71 cases of tuberculous meningitis had survived.

Many medical journals before 1939 were printed in what is now the Eastern Zone; arrangements have been made for publishing many of these journals in Western Germany, or, if this has been impossible, a new journal has arisen in place of the old. The *Archiv für Schiffs- u. Tropenhygiene*, for instance, exists no longer, but to replace it there now appears a new *Acta Tropica*. New medical books are also being published embodying the experiences gained during the war. One important work on hunger oedema gives many interesting facts which will be new to medical men in this country. Incidentally, children now seem to be well nourished and full of energy, and, apart from returned prisoners of war, the only signs of malnutrition still visible are in elderly men and women. Despite the difficult conditions under which most German doctors are working, there is a feeling of optimism and an intense desire to learn what has been going on abroad. The medical scholarships provided by the British Council are being eagerly sought. Medical research has never entirely ceased in Germany. Ultracentrifuges and electron microscopes are being produced, and new and remarkable apparatus has been devised for subjecting bacteria and viruses to ultrasonic vibrations.

Apart from outbreaks of diphtheria and paratyphoid B and some increase in indigenous cases of malaria, there has been no serious epidemic in Western Germany, though in 1947 poliomyelitis was more prevalent than for many years. Venereal disease, especially syphilis, increased alarmingly immediately after the end of the fighting, but the incidence is now decreasing.

Last year the Foreign Office published a report[1] prepared by the Medical Research Council entitled "Tuberculosis in the British Zone in Germany." While the 1946–7 figures showed no general fall in the tuberculosis mortality, there were no signs of any alarming increase. In Hamburg, for

[1] See *British Medical Journal*, 1948, 1, 508.

instance, the death rate from pulmonary tuberculosis during the post-war period has declined. It is believed, also, that the numbers of cases of coronary thrombosis and diabetes have not increased. There is much interest in the British National Health Service, especially among those engaged in medical administration, who feel that as soon as a German Government is established an analogous scheme will have to be set up in Germany.

## GRAVITATIONAL ULCERS

No doubt the erect posture is responsible for certain weaknesses in the legs of man. The location of many lesions in the leg—for instance, chilblains, erythema nodosum, and the gummatous phases of tuberculosis and syphilis—is determined to a great extent by circulatory and gravitational factors. The necrobiotic, myxoedemic, and other expressions of metabolic disturbance, and the eruptions and ulcerations which may accompany anaemia, deficiency states, and acholuric jaundice, are indications that the aetiology of diseases affecting the legs is not necessarily straightforward. Such factors should not be overlooked when considering the so-called varicose or gravitational ulcers which cause so much serious disability in the community. The condition is not limited to any one section of the community, but the incidence is greatest among those least able to rest and support their limbs—the essentials of treatment.

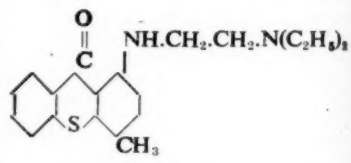
The influence of age, sex, occupation, and heredity is important, and work which entails standing with little activity may be a serious aggravation. Hypertension or arterial disease sometimes plays a part. It should be emphasized that the treatment of gravitational ulcers of the legs is an individual problem: there is no satisfactory rule-of-thumb procedure. Too much attention has been paid to the presence of superficial varicose veins. In a review of the subject in this issue of the *Journal* Dr. S. T. Anning suggests that treatment of such veins is often useless and may indeed be harmful. The value of compression and support—both still of the utmost importance—in expressing stagnant fluids was stressed as long ago as 1676 by Richard Wiseman and again in 1783 by Michael Underwood.[1] "Put the hydraulics right, and the ulcer will take care of itself" was a phrase used by Dickson Wright,[2] whose advocacy of these measures, including the use of elastic adhesive bandages for support, has not had the wide support in general practice which it deserves.

Dr. Anning finds that in the majority of patients (88.6%) the venous insufficiency affects all the tissues of the limb and is a result of thrombosis of the deep veins. This may be followed by recanalization, but as a result of damage to the valves in these veins and in the vessels communicating with the superficial veins there is grave functional incompetence, stasis of lymph and blood, and oedema and consequent devitalization of tissue. Phlebography may indicate much of this and should be undertaken before interfering with any superficial varices. In this condition the ulcer is a complication, not the essential abnormality. There is some place for methods of treatment which assist the ulcers to heal, but most emphasis should be on prevention. Whatever use is made of temporary expedients, effective support of the limb to counter the venous insufficiency and stasis should be an essential part of the permanent routine—for life in most cases. The many books and papers on this subject in the last 20 years have not been very fruitful. Dr. Anning's observations may help to direct attention from the floor of the ulcer and from the superficial veins to the underlying condition.

[1] Quoted by Adamson, H. G., *British Medical Journal*, 1931, **1**, 284.
Wright, A. Dickson, ibid., 1930, **2**, 996.

## THE MIRACILS AND SCHISTOSOMIASIS

Until the second decade of this century there was no specific remedy for schistosomiasis, though emetine had for some time been used as a secret remedy in Egypt; then McDonagh[1] and Christopherson[2] independently showed the value of tartar emetic. There was little further advance in the treatment of schistosomiasis for nearly 30 years, though attempts were made to overcome the toxicity of tartar emetic by the introduction of tervalent antimonials such as "stibophen" and "anthiomaline"; these compounds, though less toxic, were less effective. There was much interest, therefore, when at the end of the war it became known that a new series of preparations had been synthesized in Germany by Dr. H. Mauss at Elberfeld. The compounds are known as the miracils—A, B, C, and D. Miracil A is 1-diethylaminoethylamino-4-methylxanthone; in miracil B a chlorine atom is introduced into position 6 of miracil A, and the formula is therefore 1-diethylaminoethylamino-4-methyl-6-chlorxanthone; miracil D, the structural formula of which is here shown, is 1-diethylaminoethylamino-4-methylthioxanthone; and in miracil C the thioxanthone group is replaced by xanthydrol. The most promising of these compounds is miracil D or nilodin, which was shown by Kikuth, Gönnert, and Mauss[3] to be active against *Schistosoma mansoni* in mice. Its pharmacology has been studied by Wood,[4] Hawking and Ross,[5] and Kikuth and Gönnert.[6]




Miracil D cannot be injected, because of the local irritation and necrosis which it causes: by mouth mice tolerate up to 0.3 g. per kg. of body weight, the LD50 (the dose which is lethal for 50% of the animals tested) being 0.5 g. Rabbits tolerate 0.2 to 0.6 g. per kg. without harm, but death occurs after doses of 0.7 to 1.0 g. per kg. In monkeys oral doses of 0.2 g. and 0.4 g. per kg. cause slight diarrhoea, and doses of 0.4 g. and 0.8 g. produce vomiting. Miracils A, B, and C are more toxic for monkeys. In mice infected with *Schistosoma mansoni* miracil B is superior to all the others, but in monkeys it has a curative

[1] *Biology and Treatment of Venereal Diseases*, 1915, London.
[2] *Lancet*, 1918, **2**, 325.
[3] *Naturwissenschaften*, 1946, **33**, 253.
[4] *Quart. J. Pharm.*, 1947, **20**, 31.
[5] *Brit. J. Pharmacol.*, 1948, **3**, 167.
[6] *Ann. trop. Med. Parasit.*, 1948, **42**, 256.
[7] *Acta trop. Basel*, 1947, **4**, 21 and 97.
[8] Vogel, H., and Minning, W., *Ann. trop. Med. Parasit.*, 1948, **42**, 268.
[9] Watson, J. M., Abdel Azim, M., and Halawani, A., *Trans. R. Soc. trop. Med. Hyg.*, 1948, **42**, 37.
[10] Abdel Azim, M., Halawani, A., and Watson, J. M., *Lancet*, 1948, **1**, 712.
[11] Halawani, A., Watson, J. M., Nor El-Din, G., Hafez, A., and Dawood, M., *J.R. Egypt. med. Ass.*, 1948, **31**, 272.
[12] Blair, D. M., Hawking, F., Meeser, C. V., and Ross, W. F., *Brit. J. Pharmacol.*, 1949, **4**, 68.

effect only when given in doses which cause vomiting, and miracil D is the best preparation. Miracil A, which is only slightly active in mouse schistosomiasis, is more active in monkeys, and miracil C takes an intermediate position both in mouse and monkey tests. All the miracil compounds have a remarkably poor action on immature worms. Even with optimum dosage, however, adult worms do not begin to die until about 14 days after the administration of the drug is begun, but egg production is disturbed within a very few days, as is shown by the formation of eggs without shells, of deformed eggs, and of conglomerations of shells and yolk cells, as well as by the excretion of large drops of shell substance. These changes are associated with degenerative changes in the cells of the testes, ovaries, and yolk-glands and are similar in character to those observed by Vogel and Minning[7] in *S. japonicum* when acted on by tartar emetic, stibophen, and emetine. Curiously enough, none of the miracils has any action whatever on experimental infections due to *S. japonicum* in rabbits, hamsters, and monkeys.[8]

Because of the results obtained in animal experiments, miracil D was selected for clinical trials, and tests have now been carried out in Egypt[9-11] and in Southern Rhodesia.[12] In Egypt doses up to 7.5 g. were given in eight days to patients with *S. haematobium*. With the highest doses permanent cures were usually obtained, but there was some evidence of toxicity. The blood concentration of miracil D, and presumably its toxicity, are raised when the renal functions are impaired. In Southern Rhodesia daily doses ranging from 35 to 150 mg. per kg. of body weight were given to boys and young adults for 10 days. Fifteen weeks after the end of treatment 12 of 18 patients appeared permanently cured. For reasons not yet explained symptoms of toxicity were much less pronounced than in Egypt and consisted mainly of abdominal pain, nausea, vomiting, slight disorientation, and cough. The frequency of these symptoms was not related to the size of the dose and seemed to depend, at least partially, on personal idiosyncrasy. Very occasionally herpetiform eruptions are seen both with miracil D and with tartar emetic; possibly, therefore, the condition may be due to allergy from disintegrating schistosomes rather than to drug toxicity.

*S. mansoni* seems to be less sensitive to miracil D than *S. haematobium*. In Southern Rhodesia only 1 of 14 patients was cured. In Egypt results are difficult to evaluate because of the small number of patients treated and the numerous dose schedules employed. Blair and his colleagues[12] treated a few patients suffering from urinary schistosomiasis with either miracil A or B. No cures were obtained, but the drugs were not toxic and larger doses might have been effective. Because of the poor results in animals infected with *S. japonicum* it is questionable whether the miracils will be of value in this infection. Although the optimum dose schedules for urinary schistosomiasis have not yet been established, it is obvious that, at any rate in the case of miracil D, a satisfactory alternative to antimony has been found. As a result of the ease with which the drug can be given by mouth, trials are now being carried out on a large scale in particular areas in order to try to break the cycle of infection.

## PLANT SOURCES OF CORTICAL HORMONES

Although the treatment of rheumatoid arthritis by "cortisone" ("compound E") must still be regarded as experimental,[1] there is naturally great interest in any method of increasing supplies of the substance. Not only is the present output limited to about 200 grammes per month, but the permanent limitations of the present method of partial synthesis from desoxycholic acid can be judged from the fact that it would be necessary to use the bile acid from forty cattle to obtain the 100 mg. needed daily for the treatment of a single patient over one year. The adrenocorticotropic hormone is equally difficult to obtain in quantity. According to the Armour Laboratories in Chicago, approximately 1,360 hog pituitary glands weigh one pound and only about 1½ g. of ACTH can be extracted from this quantity. All the hogs slaughtered in the United States would not yield much over a pound a week. There is also a growing interest in the cortical hormones generally, and an increasing need, therefore, for some alternative source of supply. According to an announcement[2] reported to have been made last week by representatives of the U.S. Public Health Service and the Department of Agriculture such an alternative source has now been found in sarmentogenin, a substance which was isolated in 1915 (but not then determined) by Jacobs and Heidelberger, of the Rockefeller Institute for Medical Research. The discovery was made during the investigation of seed samples from the plant genus *Strophanthus*, from which strophanthin is derived. The sample in question was a commercial one and was wrongly labelled as from the species *S. hispidus*—one of those used by African tribes as a source of arrow poison. None of the original seeds had been kept, and it was only after a number of years that another sample was obtained —this time from seeds of *S. sarmentosus*—which yielded the same substance. The plant is a tropical vine which may grow to a height of eighty feet or more. Besides growing in Africa, it is found also in India, Burma, the East Indies, and the Philippines.

More recently it has been shown that with sarmentogenin as the starting-point cortisone can be prepared with 20 intermediate steps instead of the 37 the present method entails, and that a ton of seed could provide enough cortisone to treat one patient for a year. This would be a useful simplification, but still a long way from an ideal method of manufacture. Although both seeds and plants have been collected from Liberia by an expedition led during the present summer by Dr. J. T. Baldwin and sponsored by the Federal Security Agency and the Department of Agriculture, it is pointed out that five years would be needed before plants raised from seed would be in bearing. None the less, the project of large-scale cultivation under equatorial conditions is being contemplated, and a further appropriation is being sought for a wider investigation of plant sources of animal hormones. If the therapeutic value of cortisone as at present prepared is established, then its preparation on a larger scale will become more practicable. Further, the partial synthesis of other cortical hormones may be simplified.

[1] *British Medical Journal*, 1949, **2**, 24 and 154.
[2] *New York Times*, Aug. 16 and 17, 1949.

## THE MENTAL HOSPITAL POPULATION

### BOARD OF CONTROL REPORT

An account of the mental health services of England and Wales was recently for the first time incorporated in the annual report of the Ministry of Health (*Journal*, Aug. 13, p. 381). To satisfy a provision of the Lunacy Act, however, an annual report has to be made by the Board of Control to the Lord Chancellor, and this, which has just been issued, contains some further details. The number of persons under care under the Lunacy and Mental Treatment Acts at the end of 1948 was 144,725, of whom 140,915 were in hospitals now vested in the Minister of Health. The designation of mental hospitals is said to have proceeded smoothly in spite of complications resulting from the fact that many former public assistance institutions were continuing to accommodate mental patients and a good deal of sorting out had to be done and is still continuing. On the basis of recognized standards there is considerable overcrowding in the former county and county borough mental hospitals, and it was worse at the end of 1948 than it had been at the beginning of the year. The main problems are shortage of staff, unreleased beds, and lack of new building. The nursing shortage has been somewhat ameliorated by the recruitment of part-time nurses, though it is hinted that this arrangement is not altogether satisfactory in mental hospitals. But according to the reports of the individual commissioners who have made statutory visits to various institutions the shortages have not adversely affected the welfare of the patients, thanks to the efforts of the medical and nursing staff, to whom the Board pays a tribute.

The death rate in 1948 was 6.26% of the average number resident, being 1.36% below the rate for the previous year. Tuberculosis continues to occur more frequently in mental hospitals than among the general community, and this year, owing to intensified methods of *x*-ray examination, there was a slight increase in the number of cases discovered, but the death-rate from tuberculosis fell from 5.5 per 1,000 patients resident to 4.7. Gastro-intestinal infections, on the other hand, are said to be more rare proportionately in the mental hospitals than outside them. Less than one patient in a hundred is so affected, and the death rate is less than one per 10,000 persons resident.

In the view of the Board the documentation of certified patients continues to be unsatisfactory. In one quarter of 1948 an investigation was made, and it was found that, out of 6,156 documents for temporary and certified patients received, 384 had to be returned for amendment on medical grounds and 1,291 for amendment for technical reasons; ultimately in each category 55 were rejected.

From the tables which appear at the end of this brief report it is shown that in the designated mental hospitals and the teaching hospitals there are 60 Health Service patients to one private patient, but in premises not vested in the Minister the proportion is reversed. There was a large decrease (over 7,000) in the number of private patients during 1948 and a corresponding increase in the number of Health Service rate-aided patients. The number of voluntary patients in hospitals and under care of all kinds was 21,788 and of certified patients 123,464. Of the total number of persons suffering from mental disorder and under care about 57% are females, who predominate in every category, except that of Broadmoor patients. The Broadmoor population is just upon 1,000, of whom only one-fifth are women.

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The Ministry of Food has reminded retailers that where an additional quantity of butter and margarine together is specified on Form R.G.48 issued to diabetics the *maximum* amount allowed is 10 oz. of butter and 10 oz. of margarine. This means that diabetics are entitled each week to 6 oz. of extra butter and 6 oz. of extra margarine in addition to the normal weekly ration of 4 oz. of butter and 4 oz. of margarine. Margarine may be taken in lieu of all or any part of the butter ration.

# Nova et Vetera

## WILLIAM WALWYN, "HEALTH'S STUDENT"

The name of William Walwyn is as familiar to the political and social historian as it is unknown to the medical historian. This is not surprising, for only in recent months has the celebrated leader of the "Levellers," the associate of Lilburne and Winstanley, been identified with the obscure unlicensed practitioner who wrote *Physick for Families*.

Many of our younger historians are making a special study of the English Puritan revolution. One of the most recent products of this revived interest is a book[1] by Dr. W. Schenk, lecturer in economic history at Exeter. The third chapter of this book is devoted entirely to Walwyn, and Dr. Schenk's account supplements and corrects the entry in the *Dictionary of National Biography* in many particulars.

Born in 1600[2] at Newland, Worcestershire, William was the son of Robert Walwyn, gentleman, and of Elizabeth, daughter of Herbert Westfaling, Bishop of Hereford. After apprenticeship with a silkman in Paternoster Row he became a member of the Merchant Adventurers' Company and maintained a large family "in a middle and moderate but contentful condition." One of his daughters married Humphrey Brooke, F.R.C.P., who may have influenced Walwyn in the choice of his later career and whose own written works reflect the influence of Walwyn's social and religious views.

Walwyn's career between 1642 and 1649, when he spent eight months in the Tower with Lilburne, accused by Cromwell of fomenting mutiny in the Army, belongs to English history and is adequately dealt with by Schenk.

### "Physick for Families"

While working on his book in the Bodleian Library, Dr. Schenk came across the 1681 edition of *Physick for Families*, by William Walwyn, which has a portrait frontispiece, engraved by R. White, of the author at the age of 80.[3] Collating this with the information given in the Newland parish register and in a published pedigree of the Walwyn family,[4] which states that William Walwyn, M.D. (*sic*), of London, son of Robert Walwyn, of Newland, married and had several daughters and died *circa* 1680, Schenk identifies the author of the book with Walwyn the Leveller. Final confirmation was given by the discovery of Walwyn's will in Somerset House. This is dated 1680 and was proved on Jan. 14, 1681.

Schenk seems to be unaware of any other medical book by Walwyn or of any other edition of the *Physick for Families* (which he thinks was published posthumously and possibly commemoratively), so that his account of Walwyn's medical career is necessarily vague, although there is evidence in the 1681 edition of the *Physick* that Walwyn may have been practising as early as 1665, during the "great Mortality." It is no reflection on the thoroughness of Dr. Schenk's researches that his results were so limited in this respect, for the 1681 *Physick* is indeed the only medical book with Walwyn's name on the title-page. Apart from the Bodleian copy there is one at the Royal Society of Medicine; copies of a 1696 edition are to be found in the British Museum and in the Army Medical Library at Washington. But there *were* earlier editions—one in 1669, presumably the first; and another in 1674. Both editions are in the Wellcome Historical Medical Museum and in the Cushing Collection in Yale Medical Library. In addition, there is a book called *A Touchstone for Physick* published anonymously in 1667, copies of which survive in the British Museum (catalogued

[1] *The Concern for Social Justice in the Puritan Revolution.* London, Longmans, Green, 1948. Pp. 41–63.
[2] According to the Newland parish register he was baptized on Aug. 17, 1600. *The Dictionary of National Biography* has (fl. 1649) and its account does not go beyond the year 1651.
[3] This portrait is reproduced as the frontispiece of Dr. Schenk's own book.
[4] *Visitation of the County of Worcester, 1682–83.* Edited by W. C. Metcalfe. Exeter, 1803, p. 100.
[5] *Dictionary of Anonymous and Pseudonymous English Literature*, 1926–34. Vol. 6, p. 65.

under W. W.) and in the Wellcome Historical Medical Museum. This work is correctly attributed to Walwyn by Halkett and Laing.[5]

It is thus possible to state that Walwyn was practising medicine certainly before 1667, and there is internal evidence that he was practising for some years before his *Touchstone* was published. On page 81 he declares that the value of his medicines had been proved

> "even in the Pestilence it selfe, for though I staid not in London past the increase of two Thousand a Week; but was forced away or must be cruel where all obligations of tenderness lay upon me: yet took I care that nothing of mine should be wanting to any, who desired to make use of them; with some liberty of freely helping the necessitous: besides I had long declined Practice, visited none, nor had then so much as one Patient under my Hand: and withall had so published the Vertues and Uses of all my Medicines; as sufficed both to encourage and to instruct every one so plainly, as without further direction or attendance, every one might be in a capacity of helping themselves and their relations upon any occasion."

On page 84 he refers to "one who practised much with them [his medicines] long before, and from the beginning to the ending of that sad Mortality." The preface to the book is signed W. W., and at the end is the address, "At the Star in the Postern by little Moorefields, London, 1667."

The 1669 edition of his *Physick for Families* is also anonymous, but the preface is signed "W. W. Healths Student" from the same address. The 1674 edition has his initials and address on the title-page, and begins, without preface: "Having now past through many years Practise, in this my new way of Physick; And with God's blessing in, and upon my peculiar Method and Medicines, been most happily successefull, in abundance of very threatning, dangerous Distempers. . . ."

### Walwyn's Method and Medicines

What were his "peculiar method and medicines"? The answer to this question fills the last gap in our knowledge of Walwyn and of his career as reformer and physician. They consisted of an uncompromising repudiation of all the fashionable medical procedures of his day, such as purging, bleeding, vomiting, issues, clysters, and the indiscriminate exhibition of mineral drugs, and the renunciation of polypharmacy and all the evil-smelling and foul-tasting mixtures which made up the greater part of the seventeenth-century pharmacopoeia. He advocated a mild expectant treatment, aided by the patient's co-operation and his own "peculiar medicines," which were 32 in number, each one appropriate for a particular "mark or character of disease." He does not tell us what went into these medicines, but assures his readers that they were all pleasant to the sight, smell, and taste, liquid in form, and generally of a clear and sparkling character.

His books largely consist of case histories in which the virtues of his treatment are vindicated by a successful outcome. He informs us that he declined "the common Road of Physick" (he had no medical qualification) for no other cause "but for its manifest uncertainty in Principles, Roughness, Harshness and Cruelty in Methods, Impropriety, Impotency and danger in Medicines." Instead, he sought to blaze his own trail as a "Healths Student," probably influenced by his son-in-law, Humphrey Brooke, whose book *A Conservatory of Health* (1650) stresses the value of preserving health rather than curing disease.

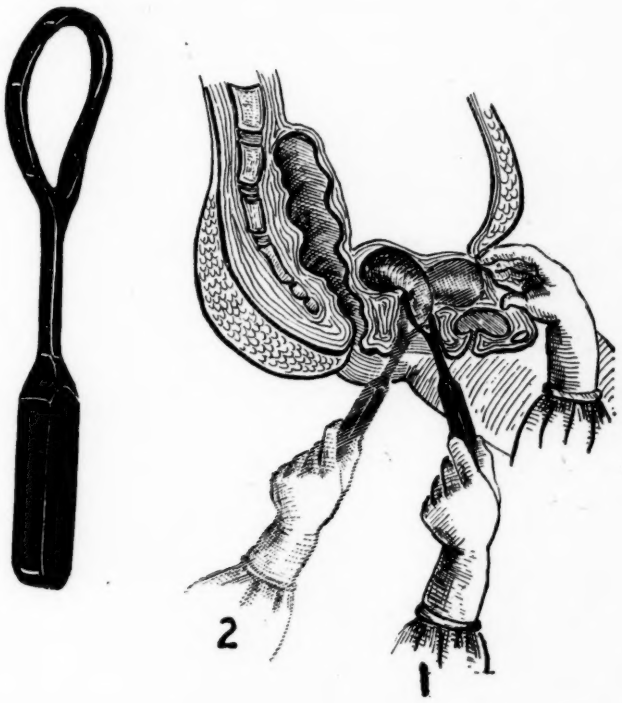
The medical historian, while introducing a new figure into the gallery of medical men who have left their mark on history, and while applauding the originality which led Walwyn to reject the therapy of his day before the scientific reasons for such a rejection were enunciated, may yet criticize the unscientific character of his books. Walwyn gives his own answer: "I conceive my charitable intentions sufficiently justified by the Text: The truly Christian Vertue of *Compassion*, being as essentially needful in a Physitian, as in the most tender hearted Samaritan."

F. N. L. POYNTER.

# Preparations and Appliances

## UTERINE ANTEVERTOR

MR. MCKIM MCCULLAGH, surgeon, Samaritan Hospital, London, writes: For those elect few among general practitioners, consultants, and specialists in gynaecology who believe that a fully retroverted uterus can cause such symptoms as backache, dyspareunia, menorrhagia, premenstrual depression, headaches, and even nausea, not to speak of sterility and miscarriage, I can recommend the antevertor depicted in the diagram and made by A. L. Hawkins, Ltd., of 15, New Cavendish Street, London, W.1, as a helpful instrument.




Normally one endeavours to antevert the uterus with the fingers by pushing upwards in the posterior fornix and then changing the finger-tips to the anterior fornix and pushing the cervix backwards. The left hand is kept on the abdomen ready to contact the fundus uteri and pull it forward. For those with short fingers the procedure is difficult, especially in a patient with a long vagina. A long narrow Hodge pessary grasped by the thumb and first two fingers at its lower end is often used to transmit the push to the posterior wall of the corpus uteri, which causes it to move forward and upward from the floor of the pouch of Douglas.

The vulcanite antevertor here depicted saves the patient some of her discomfort and the specialist mental and physical strain. It is easy to introduce and use, and causes no pain or pressure at the vulval orifice. The lift and degree of pressure on the posterior fornix are easily regulated, as the handle of the instrument is well outside the vulva and is used as if it were the handle of a long spoon. The lift and pressure on the posterior wall of the uterus should be as high in the posterior fornix as possible, and it should be slow and gradual and always short of causing appreciable pain to the patient. I find anteversion of the uterus much easier to attain with the antevertor than with the fingers or a Hodge pessary. When anteversion is attained and the uterus pulled and flexed well forward, a suitable Hodge or ring pessary is inserted. After three days a marked improvement in comfort and mental outlook frequently follows and definitely warrants the advice of surgical treatment in the form of a ventrosuspension operation.

# Reports of Societies

## FRIENDS OF THE HEBREW UNIVERSITY

### London Dinner

The Friends of the Hebrew University held a dinner at the Park Lane Hotel on July 21 to celebrate the opening of the new medical school in Jerusalem. Professor SAMSON WRIGHT, who presided, remarked that the representative gathering reflected the widespread interest in this country in the new institution. He had received many messages of good will, including one from Sir Henry Dale, who had expressed his high hopes of the school. Professor Wright pointed out that the annual budget of the Hebrew University was now some £700,000. The Government of Israel made a grant of £50,000, but the large balance had to be raised by friends all over the world. He referred to the help received from British research funds, and he thanked the British Government for granting the University facilities to acquire surplus scientific equipment on generous terms. He hoped that the dinner would mark the re-establishment of the cordial relationships which had always existed between the Hebrew University and the British scientific, academic, and medical world.

The Minister of Israel, Dr. MORDECAI ELIASH, said there were some 3,000 doctors in Israel to serve a population of less than a million, or roughly three times as many doctors as are required by an ordinary community. During the first five months of this year 500 doctors had arrived in Israel, which, taking full account of the immigration during that period, still maintained the proportion. But most of these doctors had passed the prime, and the number of young practitioners was alarmingly small. On the other hand, the number of hospital beds was still much below the normal requirements of the country, only 3,000 being available instead of the normal eight or nine thousand.

For some years there had existed a pre-faculty of medicine of the Hebrew University of Jerusalem. In the year 1946–7 appreciable progress had been made and a new building was laid down on Mount Scopus. On May 17, 1949, the first 45 students from among 200 applicants were enrolled. They were mainly Israel medical students who were recalled from abroad to serve in the Army. The medical school would be the best memorial to the three men—Dr. Yaski, Dr. Doljanski, and Dr. Ben-David—who were its leading planners and who lost their lives in the Mount Scopus massacre in April of last year.

Sir HENRY COHEN referred to his life-long connexion with the Hebrew University, of which he was a Governor. He paid tribute to the work of the University hospital staff and its scientific workers in coping so successfully with the grave problems resulting from the prolonged siege and military operations in Jerusalem. He commented on the meagre salaries now paid to the academic staff of the University, and hoped that resources would soon be available to enable their remuneration to be raised.

Dr. REDCLIFFE SALANSON, F.R.S., proposed the toast of the guests, who included Lord Horder and Dr. H. E. A. Boldero. Dr. ARTHUR FELIX, F.R.S., responded.

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Next month the Manchester Municipal College of Technology is to begin a series of evening courses for laboratory technicians. These courses are intended to supplement their daily work in the laboratory and to help them prepare for their professional examinations. Both scientific and medical subjects will be taught. There will be an intermediate course in the elements of laboratory technique in pathology, bacteriology, chemical pathology, and haematology, and four independent final courses in each of these subjects. At the end of the final course the student will take the corresponding final examination of the Institute of Medical Laboratory Technology.

# Correspondence

## Distinction Awards

SIR,—The very important letter from Dr. F. M. R. Walshe (Aug. 13, p. 383) is not likely to go unanswered, but the signatories of this letter, all members of the consulting staff of a teaching hospital, wish to express their whole-hearted agreement with everything said by Dr. Walshe. As he pointed out, the Awards Committee has a wholly impossible task, and it seemed only too probable that in an attempt to solve their problems they would be compelled to adopt methods of obtaining information which are both undesirable and invidious. There can be no doubt that consultants are not all of equal merit and that therefore some are worthy of special distinction. We would submit, however, that the academic distinctions of the past will remain in operation (the Member of the College will strive for the Fellowship, the Fellow may be elected to the Council), and private practice still remains at the disposal of those who feel that their merit deserves remuneration.

We hope with Dr. Walshe that it is not yet too late to abandon the idea of distinction awards in its present form.—We are, etc.,

R. BROOMHEAD.
J. LE FLEMING BURROW.
J. M. P. CLARK.
ANDREW M. CLAYE.
DAVID W. CURRIE.
HUGH GARLAND.
F. F. HELLIER.
BRYAN JEAFFRESON.
A. J. C. LATCHMORE.
IAN MACPHERSON.
H. H. MOLL.
MICHAEL C. OLDFIELD.
A. B. PAIN.
LESLIE N. PYRAH.
GEORGE SEED.
H. S. SHUCKSMITH.
H. W. SYMONS.
MAXWELL TELLING.
J. M. LEES.

Leeds.

SIR,—Not only teaching-hospital committees but committees for professional assessment in hospital regions have been asked for recommendations for merit awards, and, difficult as the job is, it is being tackled. What is the alternative? How are consultants to be paid? To reject the considerable sums of money offered would be hard on some men. The method of distribution put forward by the Spens Committee at the suggestion—it is understood—of a distinguished layman is supported in principle by the Consultants and Specialists Committee of the B.M.A.

The range of qualities and skills among consultants is of course vast, and grades do not exist except in the mind of the observer. In the past incomes have been vastly variable also. But can we say, when we look at the incomes tabulated in the Spens Report and remember able men earning much less than they deserved, that the old method was really good? When we remember such men, surely we grade them in our minds, just as we have always graded fellow consultants, though not by finding out who earns the most, when sending our patients—or taking our relatives and ourselves—to them.

In spite of philosophical doubts, then, if we are honest with ourselves we admit we have acted as if grades existed, though we have gone to some trouble to conceal the fact. We are now asked to express the opinions which guided us up to July 5, 1948. It is not easy: if another method of letting consultants get what they need can be produced nobody would be more glad than I. But to reject this scheme without producing one as good, or at least feeling sure that the method that worked before the Health Service began would work better now, is to do something very drastic. All political parties are determined on a health service, and it happens that in the one proposed to us a consultant is rewarded less according to his prestige with the laity and more according to the opinion of his fellows. It is a defensible point of view.

The decisions ought not to be made by only a few, however, and it seems from information given to regions that they will not be. Recommendations will come from several directions and be referred in several directions again. One direction from which they will come (and on this the Consultants and Specialists Committee has been emphatic) must be local. It

is impossible to judge without local knowledge. But this, we understand, is only one source of information : to place sole responsibility there would be too heavy a task altogether, and we do not think it is contemplated.

For this responsibility is deeply felt. People who accept it do so because they believe the profession is faced with political and economic facts which can only be ignored to its certain disadvantage, and they are not prepared to ignore them. If consultants as a whole refuse extra pay then assessment committees can rest at last. But unless consultants do refuse the money the committees must do their best.—I am, etc.,

Hove, Sussex. W. A. BOURNE.

SIR,—Dr. F. M. R. Walshe (Aug. 13, p. 383) has again done a great service to our profession by attacking the whole conception of distinction awards, but he has ignored at least two of its weaknesses. First, if recommendations are to be made by subcommittees of hospital medical committees it seems clear that the members of such subcommittees will have to be chosen from among those who are considered to be unsuitable for a merit award—an invidious task for the chairman of the medical committee. Secondly, as chairman of the medical committee of a non-teaching hospital I have not received one of the signed circular letters. Is it to be assumed, therefore, that only the staffs of teaching hospitals are eligible ?

There have been previous attempts to weaken the precarious unity of the medical profession : they failed. Let us be careful that the bait of financial benefit does not split the consultants into envious groups.

If there is, indeed, some money available it could be employed in a much more fruitful way. Thus we were promised that anybody would be allowed to use the whole of the facilities of the N.H.S. or any part of them. Since then the Minister has refused to allow private patients to use that part of the service that consists of receiving free drugs, using as his excuse the nonsensical statement that medical advice and treatment cannot be separated from one another. Oddly enough, he does not hold that this indissolubility holds in surgery : everyone is entitled to be a private patient and yet to be operated on gratuitously in hospital. It is, I think, impossible to escape the conclusion that the Minister thinks that the granting of the right to receive medicines without direct payment for them would wreck his scheme, because so many people would choose to be private patients.

Whether this would be so or not is a matter of opinion and need not be discussed at the moment. What is, however, relevant to my remarks is the reply of Mr. Blenkinsop to Mr. H. D. Hughes (*Journal*, Aug. 13, p. 393). He said that if the estimated annual rate of expenditure on the pharmaceutical services were proportionately increased in respect of the 5% of the population not on doctors' lists the increase would amount to about one million pounds. If this expenditure were undertaken private practice would undoubtedly revive. And consultants would do as they did in the past—they would build up practices. Then the various kinds of "distinction" in medicine would have their chance to add to their possessors' incomes, while the Distinction Awards Committee, having no part to play in assessing the status of members of a learned profession, could be disbanded.—I am, etc.,

London, W.1. A. PINEY.

SIR,—I hope that Dr. F. M. R. Walshe's admirable letter (Aug. 13, p. 383) will rouse us to action. The vast majority of doctors consider the distinction awards a ludicrous suggestion, and it is well recognized that an equitable manner of selection of individuals to receive such awards is a frank impossibility. It seems incredible that members of what has been for so long an honourable profession should become commercialized so rapidly that they may be willing, as Dr. Walshe aptly says, "to be priced as though they were professional soccer players." Must distinction in our profession now be assessed only in terms of pounds, shillings, and pence paid through a Ministry ?

In the eyes of the general public our professional prestige has already been sadly dimmed by what appears to be our undue concentration on the monetary side in our negotiations with the Ministry. Are they now to be diverted by the spectacle of those who should be the leaders of our profession sitting in solemn conclave dispensing first-, second-, and third-class distinction awards, payable in cash, to their colleagues ? We expect a better moral lead from those in high places.

I have the honour to sit on two committees to which the request from the chairman of the Distinction Awards Committee has been made for guidance. Cynical laughter is the instant reaction in any medical group where the subject is mentioned. Nevertheless, when it is suggested that we shall have nothing to do with this farcical plan, fears are expressed that by inaction we may be doing an injustice to colleagues in our own hospital or specialty and that other bodies may make recommendations although we refuse.

Surely it is high time that we ceased to be guided by such a policy of expediency. These fears of possible consequences have insidiously broken down too many of our defences already ; they are all too reminiscent of the successful Nazi method of producing an attitude of cynical defeatism. If, as individuals, we feel a policy is wrong we ought to have no hesitation in making a stand now against a scheme which must lead inevitably to jealousy, suspicion, and discord among members of our profession. As individuals and as members of any professional body to which we may belong we should rouse ourselves from a state of apathetic acquiescence and protest against this attempt to put a financial value on that invaluable and indefinable thing—professional distinction.—I am, etc.,

London, N.W.1. KATHARINE LLOYD-WILLIAMS.

## Poliomyelitis Precautions

SIR,—In your leading article (Aug. 6, p. 323) you advise doctors to keep children at home who are suspected of being in the pre-paralytic stage of poliomyelitis. I feel that this is an unwise recommendation, for it is very liable to cause delay in the diagnosis of meningitis, particularly tuberculous, which is very apt to be confused with poliomyelitis in the early stages. The prognosis of tuberculous meningitis depends largely on early diagnosis.

Only last week a child was admitted to this hospital in deep coma as a result of tuberculous meningitis : he had been watched at home for a fortnight as a suspected case of poliomyelitis. In my opinion a case of suspected poliomyelitis, especially if there is meningism, should be admitted immediately to hospital for investigation.—I am, etc.,

The Children's Hospital, Sheffield. J. LORBER.

## What is Social Medicine ?

SIR,—May I say that I have long shared Dr. Thomas Gibson's uncertainty (Aug. 13, p. 388) as to the meaning of the term "social medicine," and have asked repeatedly and in vain for a satisfactory definition. If Professor W. Hobson's extremely comprehensive description (July 16, p. 125) is accurate, then surely the term "psychosocial medicine," which is already in use, would be the more appropriate.

But my difficulty here is that a few years ago, when a "strong" subcommittee of a famous hospital was considering an appointment in this "new" specialty, neither its department of public health nor its department of psychological medicine was represented on the subcommittee or consulted in any way on the matter.—I am, etc.,

London, W.1. HENRY YELLOWLEES.

## Conceptions of Right and Wrong

SIR,—The question of the adequacy of the M'Naghten rules to express or interpret modern knowledge on the subject of responsibility is raised afresh and in a prominent form in your report on the Haigh trial (July 30, p. 286).

As is generally known, the two questions requiring proof in any individual case in which the subject of responsibility is

raised are that the accused person was not aware of the nature and quality of the act he was doing or that he did not know that what he was doing was wrong. I would very much like to be authoritatively informed of the meaning of the word "wrong" in this context. My opinion is that it has been generally employed to signify wrong in the moral sense, the meaning that the average rational individual in this country—i.e., living in our particular form of culture—would give it.

But the prosecuting counsel, Sir Hartley Shawcross, at the Haigh trial gave a different interpretation to the term. He is stated to have put to the medical witness the question: "I am not asking you whether the man decided, in obedience to a higher power, to do what he realized was wrong; I am asking you to look at the facts and tell the jury whether there is any doubt that he must have known that, according to English law, he was preparing to do, and subsequently did, something which was wrong." I submit that this is not the meaning of the word "wrong" intended by the M'Naghten rules. I say this because, in the first place, there have been many trials in which it has been interpreted in the ordinary moral sense. A not uncommon example is the case of the mother who in a state of depression kills her child in order to save it from the suffering she imagines is in store for it. She may be aware of what she is doing, may know that it is against the law and that she will be punished for it, but she considers it right and justifiable in the light of her strong (abnormal) convictions.

In the case of M'Naghten himself, from what is known of his state of mind we can draw the highly probable conclusion that he knew what he was doing when he shot Sir Edward Drummond and also that he knew that "according to English law" what he was doing was wrong. At the same time his judgment of right and wrong was so impaired by his delusions of persecution that it was obvious to the court that he was of unsound mind. If, however, the same test had been applied to him as was applied in the case of Haigh, M'Naghten would not presumably have been found insane at the trial.

In the second place it is to be noted that the statement of the two tests setting out the legal conception of responsibility contains the disjunctive "or" (did he know the nature and quality of the act or (*sic*), if he did know it, did he know that what he was doing was wrong). The disjunctive implies that there is a significant difference between the two tests. But the fact is that in the great majority of cases in which the prisoner knew what he was doing he would also know that what he was doing was wrong "according to English law." He may, nevertheless, firmly believe that what he was doing was right according to his conscience and his own conception of right and wrong.

It is clearly a matter of great importance to know, without equivocation, what is meant by "wrong" as used in the M'Naghten rules. It can hardly be seriously contended that it is justifiable to allow it to signify wrong according to English law in one case and morally wrong in another.—I am, etc.,

London, W.1. FREDERICK DILLON.

## Treatment of Infantile Gastro-enteritis

SIR,—Dr. C. Zahra Neumann (July 16, p. 132) is to be congratulated on a novel interpretation of part of the symptomatology of infantile gastro-enteritis, and further work will be needed to substantiate the hypothesis that the histamine bodies are responsible for some of the intoxication seen in this group of diseases.

The paper, however, does not support the claim made that a combination of antihistamine drugs plus sulpha derivatives are more effective than the sulpha derivatives alone. The sedative effect of "benadryl" is central in action, and this, by producing rest and sleep, would in itself reduce the general discomfort, irritating whine, tachycardia, and even prostration (many years ago injections of nepenthe were used for this purpose). No figures are given which could enable one to compare mathematically the reduction in number of stools in the two methods of treatment—the graphs given do not contain sufficient information for statistical analysis.

In the group treated by sulphamezathine alone (method A) there are 3 deaths in 42 cases; in the group treated by sulphamezathine plus benadryl (method B) there is 1 death in 40 cases. Now the percentage difference between A and B is $7\% - 2\frac{1}{2}\% = 4\frac{1}{2}\%$; but the standard error is 5.57%, and as the percentage error is less than twice the standard error there is no statistical significance between these figures. Furthermore, using the exact method of $\chi^2$ for a $2 \times 2$ table, it can be shown that the probability is 0.33, which means that we can expect this difference (of 3 deaths in 42 cases and of 1 death in 40 cases) to occur 33 times in every 100 experiments. In other words this difference in mortality is an event quite likely to occur by chance and no conclusions can be drawn from it. It is clear that much larger numbers of cases will need to be investigated before this claim can be substantiated.—I am, etc.,

London, W.9. C. A. ROYDE.

## Syringes

SIR,—Anyone contemplating the initial expense of a syringe service should note that the British Standards Institution has recommended the Luer fitting, and the specification in British Standard 1263 covers metal-and-glass as well as all-glass syringes. As a consequence, at least one manufacturer is now marketing syringes only of standard specification, and it seems likely that the Record fitting will be superseded and that in a few years replacements in bulk may be difficult.

The general adoption of the Luer fitting is obviously desirable, as pointed out by Dr. D. Gairdner (July 30, p. 282), and I am told that an attempt was made to adopt it after the 1914–18 war. The market was soon flooded, however, with cheap Record syringes from Germany, and English manufacturers had to conform in order to compete. A repetition of this is unlikely, and anyone making a stock of syringes should begin with the Luer pattern, for economic reasons as well as those given by Dr. Gairdner.—I am, etc.,

Broxbourne, Herts. T. C. BEARD.

## Essential Hypertension in Pregnancy

SIR,—Mr. John Sophian's letter (Aug. 6, p. 335) is of interest. The idea that "functional vascular spasm" is the primary change inducing hypertension, and that it is the cause of "renal cortical ischaemia" in pregnancy, when the renal arterioles are affected—or that it is the cause of the anuria occurring in elderly men with enlarged prostate in whom the greatly distended bladder has been emptied too rapidly—is unsatisfying. Attributed in the former to "sympathetic overactivity," the cause of this overactivity remains unexplained. Nor can I understand how in puerperal anuria Bowman's capsules and the renal tubules should become so greatly distended—with urine—if the condition is caused by a primary occlusion due to vascular spasm of renal arterioles. A picture of this change was given twenty years ago by Clifford White (*Proc. R. Soc. Med.*, 1919, **12**, 29), and his sections were shown on the screen at an R.S.M. meeting in January of this year. Those seeking an explanation of the cause of the acute changes in the kidney associated with oliguria or anuria, whether in the pregnant or not, should take this distension into account. My criticism of the work of Trueta and his colleagues is that nowhere in *Studies of the Renal Circulation* have I found any reference to the effect of the secretion of urine on the blood flow through the kidney. It is of fundamental importance.

Very interesting is Mr. Sophian's comment on Dr. Hingson's treatment of eclamptic patients by means of controlled spinal analgesia. In 1928 I published my first case treated with spinal analgesia (*Proc. R. Soc. Med.*, 1928, **21**, 70). It was received with scepticism. I believe it was tried, but I think more to demonstrate its unworthiness than any virtue it might possess. The mind of the demonstrator matters. I have had several similar experiences. In 1932 I treated a man who had developed anuria some time after an abdominal operation. Two injections were given at an interval of twelve hours, and the result was wonderful. It was so wonderful that I had the greatest difficulty in getting the paper published: everyone seemed to think the experience related was not true.

Finally, it was published in abridged form in 1935 (*Lancet*, **2**, 554). The patient, a farmer, is still strong and well—I see him occasionally by chance in the street.

In my view spinal analgesia acts by inducing a state comparable with shock. There is a great fall of blood pressure, and blood is not thrust into the renal medulla to maintain the obstruction to the exit of urine from the uriniferous tubules. The treatment should be induced early : there is no point in delaying. The position of the patient is important. He (or she) should be kept in the Sims position, with the foot of the bed elevated, and starved completely, with great limitation of fluid. More than one injection is usually required. In fulminant eclampsia it is better to try such a treatment than let the patient die. In post-partum anuria it is much better to do this than use an artificial kidney, for the application of the latter is vain at a time when the cortical renal cells are rotting. —I am, etc.,

Rugby. R. H. PARAMORE.

## Strangulated Appendix in Femoral Hernial Sac

SIR,—The following case report may be of interest to your readers.

A woman, aged 67, was admitted to St. Leonards Hospital on May 6, 1949, with a diagnosis of strangulated femoral hernia. She was collapsed and dehydrated, with a subnormal temperature, a blood pressure of 100/70 mm. Hg, a pulse of 120, and a respiratory rate of 28. Two days before admission she had complained of intense abdominal pain, most marked in the right iliac fossa. Vomiting began simultaneously, the vomit being first yellowish, later brownish, and, on admission, faecal in character. She had had no bowel action and had not passed flatus per rectum for three days. She had a tender lump about two inches (5 cm.) in diameter in the right femoral region; there was lower abdominal tenderness and a certain amount of distension. A diagnosis of strangulated femoral hernia was made.

At operation a longitudinal incision was made over the lump and the hernial sac was exposed and opened. The appendix was lying in the sac and was thickened, obstructed, and congested, with haemorrhagic patches on its walls. The neck of the sac was very narrow and was obviously obstructing the appendix; the proximal quarter-of-an-inch (0.6 cm.), which was inside the abdomen, was normal in colour and size. The herniated part of the appendix (two inches long) was removed, and the mesoappendix divided and ligated. The stump could not be buried in the wall of the caecum, but as there was a long mesoappendix it was buried in that structure. The sac was ligated and divided, and the femoral canal closed by suturing the inguinal ligament to the pectineus fascia. The patient made an uneventful recovery, and was discharged from hospital on May 20, 1949.

I am indebted to Dr. A. D. Morris, medical superintendent of St. Leonard's Hospital, for his advice and permission to publish this case.

—I am, etc.,

London, N.1. S. P. BOFFA.

## Torsion of Normal Fallopian Tube

SIR,—I have read the article by Mr. R. de Soldenhoff (July 30, p. 263) and Professor Lambert Rogers's letter (Aug. 13, p. 384) on the subject of torsion of the normal Fallopian tube, and I should like to add a further case to the literature.

I was called out to see a girl, aged 13, who had not yet begun to menstruate. She complained of colicky abdominal pains for the past four days, situated mainly in the left iliac fossa, and had vomited on the first day of her illness. Three weeks previously she had suffered from a similar attack which had lasted three days, and she had then felt well again. She was constipated and looked ill and toxic.

On examination her temperature was 100.4° F. (38° C.) and the pulse rate 96. Her tongue was furred and moist. Her abdomen felt soft, without any guarding, but she was tender to pressure in the left iliac fossa. A rebound phenomenon was present in both iliac fossae. Peristalsis was diminished. She was extremely tender in the anterior walls of her rectum, and she was *virgo intacta*.

The diagnosis of a lower abdominal peritonitis, due possibly to a perforated appendix or a perforated Meckel's diverticulum, was made. During the next few hours in hospital her pulse rate rose to 114 and she did not improve.

At operation there was a small amount of blood-stained fluid in the peritoneal cavity. The left tube and ovary formed an impacted reddish-blue mass in the pouch of Douglas. They were released with difficulty. The tube was gangrenous, due to two complete twists of its mesosalpinx. The ovary contained a blood-stained cyst. A left salpingo-oophorectomy was carried out, and the patient had an uneventful convalescence. Section of the tube showed it to be normal, but it was obliterated by blood.

This case is one of undoubted primary torsion of the undiseased Fallopian tube in a girl before menstruation had commenced. As the aetiology is unknown, its main importance lies in the difficulty of diagnosis, for there is no definite syndrome to recognize. Because it occurs in young people and the diagnosis is in doubt, I venture to disagree with Mr. de Soldenhoff and state that the urgency of operation is great.—I am, etc.,

Liverpool, 9. ALFRED M. ABRAHAMS.

## The Common Cold

SIR,—In the *Journal* of Oct. 2, 1943 (p. 433), I stated that as a result of psycho-analytic investigations I had come to the conclusion that the common cold always occurred in association with a particular emotional state which could be defined.

At the meeting of the International Congress of Oto-laryngology, reported in the *Journal* of July 30, Dr. E. P. Fowler (New York) said (p. 278), "In the common cold of all types an emotional factor is very likely to be the precipitating one . . . It is very common for a cold to develop on examination day or on a day of domestic upheaval, evidently due to changes in the nasal mucosa arising from an emotional cause." He added that he believed that a large number of colds were of a neurogenic type, due to overaction of the sympathetic, and that the outstanding prophylactic was emotional equilibrium.

I am glad to have Dr. Fowler's support for my theory. I am quite confident that further investigation of the common cold on psychological lines will confirm the psychogenic origin of this, up to now, mysterious and sometimes dangerous affliction.—I am, etc.,

Leeds. E. WRIGLEY BRAITHWAITE.

## Simulated Amnesia

SIR,—I have read with great interest Drs. R. E. Hemphill and J. R. Stuart's article (May 28, p. 938) dealing with simulated amnesia. Do any of us possess hard-and-fast criteria whereby malingering can be distinguished from hysteria ?

Very few of us like to use the former term in clinical practice, whereas in legal practice either the term malingerer or the implication that a state of simulated disability exists is frequently made. I take it that the reason for this is that in the majority of such cases the physician sooner or later discovers some underlying cause of worry which explains the response. This does not dispose of the technical question of evaluating the mechanisms whereby an individual symptom complex is produced and maintained—i.e., of explaining the actual pattern of symptoms. A large proportion of the major hysterical patterns can be removed in one session by persuasion. Now although this begs the question of the validity of such forms of therapy if unsupported by more fundamental help it nevertheless reinforces the impression held by many that the hysteric "could help it if he would"—i.e., could adopt a more reasonable manner of drawing attention to his need for help.

It appears to me that there are three clinical settings within which the problem of simulation or apparent simulation of, for example, amnesia can occur. (1) The constitutionally averagely endowed man who falsely states that he is ill, knowing that such is not the case. This is true malingering, and is rare in clinical practice. (2) The constitutionally endowed hysteric. In these cases we may be dealing with a prolongation syndrome or elaboration of a nucleus of true dissociative features. This in my experience is the most common clinical problem. (3) The psychotic. Amnesia occurring in schizophrenia is frequently amenable to precisely the same forms of treatment as is the case with hysteria. The more "genuine" the dissociative mechanisms the more grateful the patient. The more conscious the mechanism the more hostile the patient.

When we come to post-traumatic hysteria (neurasthenia) in which litigation is involved we frequently see colleagues in the witness box

stating opposite opinions. For the plaintiff it is neurasthenia, for the defence it is malingering or some oblique expression which implies this. War neurosis cases illustrate the same theme. Some regard the "shell shock" case as a faint heart and sometimes a coward. Others assert he is a sick man. I suggest that in many cases the truth is a combination of both statements. That is to say, when we meet conversion hysteria we can assume that the patient is in distress and to that extent a sick man, but also that mechanisms have come into play which to some extent (varying from patient to patient) are under his control.

When we say that "dissociation" occurs in hysteria we are employing a term which possesses no referrent. This is not to deny its hypothetical validity or indeed its pragmatic necessity, and it appears as if this term describes a class of event which expresses at one and the same time a reaction to emotional trauma and a constitutional capacity for dissociation which the non-hysteric does not possess.

I have seen a pseudochoric maintain his movement for eight weeks to the point of emaciation through inability to eat and sleep, resist narcosis, shock therapy, and what psychotherapy was practicable, and then recover within 12 hours following strong persuasion. I have seen a soldier going about camp with his back bent double for weeks, resist similar methods, and then respond to persuasion in the matter of a few minutes. When the law is concerned with a compensation issue the question of the extent of this control becomes important. I know of no criteria whereby this can be determined. When all is said and done we all "forget" appointments occasionally, tell white lies, lose all emotional control at times, and under stress get palpitations or feel weak at the knees. The hysteric does these things more frequently, for longer, and at times apparently more convenient to his self-interest.

If we are good physicians we do not sit in judgment on him—we seek to understand and try to help. If we are judges or commanding officers or school masters or parents we occasionally have to sit in judgment, and sometimes we reprimand. Now, can anyone deny that a reprimand benefits the hysteric?

Finally, may I reiterate the question which has prompted this letter? Can any psychiatrist assert that he can diagnose with confidence between malingering and hysteria in any individual case? Because if there is such a test medico-legal work in our compensation courts will become easy. The answer to this question would illuminate the manner in which those processes we call dissociation operate, and enable us to understand how a hysteric really thinks and feels about the world. My opinion is that the hysteric can be compared to the "double-jointed person" who possesses the faculty of contorting his frame in a manner not possessed by others. Sometimes this queer mechanism is set going by emotional trauma, and to that extent the patient is a sick person. Sometimes it is set going as a result of the patient's decision to evade responsibility or duty or to establish prejudice in his favour (as in compensation cases). More commonly it is a mixture initially outside his control which becomes prolonged and sometimes, in addition, elaborated. The elaboration features are true malingering, the prolongation features are more or less genuine, and the original nucleus is entirely genuine.

Persuasion is capable of removing the elaborative features but will rarely affect the genuine features except it be exhibited in a manner which introduces still more subtle therapeutic mechanisms. "I seemed to be unable to get better myself: I wanted to but couldn't until you seemed to get me going," as one patient (I believe correctly) assessed the effect of brisk admonitions to a previously intractable pseudochorea. Needless to say, the physician who has the temerity to attempt to treat hysteria by admonition, though invariably receiving the gratitude of his genuine patients, will encounter strong hostility from the non-genuine. Hence the need for accurate diagnosis.
—I am, etc.,

Dunedin, New Zealand. HAROLD PALMER.

## Paraffin-wax in the Male Bladder

SIR,—I read with interest Dr. T. J. D. Lane's report (July 23, p. 216) on paraffin-wax in the male bladder. I should like to mention a similar case which I encountered in Poland in 1936.

The patient was admitted to hospital with acute cystitis. Cystoscopy confirmed this diagnosis, and to my great surprise revealed a blue-tinted twisted Christmas candle floating on top of the liquid ("rivanol") which had been injected into the bladder for the purpose of the examination. I instilled about 300 ml. of pure benzine into the bladder and after 20 or 30 minutes removed this liquid. I then filled the bladder with rivanol and on cystoscopy failed to find any traces of the candle except for the wick, which I removed with the help of an operation cystoscope (Sass-Wolf). The paraffin-wax had evidently become completely dissolved. The cystitis subsided after three days' treatment by washing the bladder out with rivanol and instilling 100 ml. of silver nitrate (1 in 200). When the patient was asked if he himself had introduced the candle into the urethra, he reluctantly admitted that two days previously, while drunk, he had had intercourse with a prostitute whom he could not pay. She in her anger had inserted the candle while he was asleep.

—I am, etc.,

London, S.W.5. B. B. RAPACKI.

## Nucleoprotein, Virus, and Mouse Cancers

SIR,—Low-temperature treatment of mouse carcinoma tissue yielded remarkable results in the laboratories of the Imperial Cancer Research Fund (July 30, pp. 251, 253, 255). As to the facts, I hope they will readily obtain ample confirmation; as to the theories attached to them, however, I deem it necessary to consider further possibilities as well. May not very low temperature cause structural changes in the protein molecule itself? I refer particularly to the nucleoproteins of the chromosomes, and this altered molecule might be the causative agent of the tumours. Experimental grounds for this suggestion can be found in the Continental literature. Karuo Yamafuji and Teigen Cho (*Biochem. Z.*, 1948, **318**, 95) claimed to be able to produce tobacco-mosaic virus by keeping the plant at higher temperatures (43–45° C.) and the polyaeder virus of the silkworm by this and other means. The virus so produced seemed to be to a certain extent transmissible, without any further temperature effect. Their theory is that normal nucleoprotein becomes denaturated nucleoprotein, which becomes polymerized nucleoprotein, which becomes a virus.

Although the authors did not refer to the production of tumours in this article, the possibility cannot be left undiscussed. The following two experiments therefore appear to be necessary. (1) The same cooling procedure should be applied to non-tumour tissues, and these should be grafted into an animal afterwards to ascertain the behaviour of normal tissue protein under such circumstances. (2) Lower temperatures than −79° C. should be applied—say −150 or −200° C.—to prove that there is a low temperature which kills the virus. Without such proof the virus nature is contestable, and the possibility of a non-living agent—i.e., a polymerized molecule—is likely.

It is a puzzling observation by Dr. Mann that it is not the time of freezing but the repetition of it with corresponding thawing that causes a diminution in the infectivity of the agent. It might be that the virus is more easily killed by repeated freezing than by a prolonged spell, but the protein molecule may have the peculiarity of withstanding polymerization, becoming resistant to it on repetition. Regarding the virus, it would be strange if it is killed by the process of thawing when it is resistant to extreme low temperature. It might be equally suggested that the denaturation of some virus-inhibitory substances, the existence of which is propounded by Dr. Mann, does not take place on repeated freezing and thawing. This would be a further field of research. There are many more interesting points. They are, however, beyond the scope of a letter, which should be brought to an end by expressing a high appreciation for the experimental results which give so much food for thought.—I am, etc.,

London, N.W.2. J. KUCHARIK.

## B.M.A. Tuberculosis Group

SIR,—May I draw the attention of all old tuberculosis officers, tuberculosis superintendents, and tuberculosis physicians to the newly constituted B.M.A. Tuberculosis Group, and urge all to join it? I hope secretaries of local tuberculosis societies in England, Wales, Scotland, and Northern Ireland will be willing to help, first by getting a supply of forms from B.M.A. House and then by circulating them to their members and having copies available at all the early autumn meetings. If 90% of tuberculosis workers join the group the tuberculosis service will wander less in darkness and confusion than at present.—I am, etc.,

Church Stretton, Salop. G. LISSANT COX.

## POINTS FROM LETTERS

### Histamine Desensitization in Ménière's Disease

Dr. D. A. DRAFFIN (Newcastle-upon-Tyne) writes: Wing Commander Saville Paul (July 23, p. 216) draws attention to an interesting case of Ménière's disease which he treated by histamine desensitization, and he adds that it is reasonable to assume "that a cure has been probably effected." Surely the following errors have been made. (1) The natural history of this type of case has been ignored, for many cases of this type tend to get less frequent attacks in any case. How much improvement in this officer's morale will contribute to mitigation of the tinnitus (which he incidentally still has) is difficult to assess. (2) Faith has been placed in the histamine test. (3) The body has theoretically been desensitized to what is closely related to, if not identical with, the natural substance of the body, on which the body relies to a large extent for its defence against attacks from all sides, be it bacterial toxins, injury, or allergens.

### The Elderly Sick

Dr. W. R. E. HARRISON (Buxted, Sussex) writes: Your leading article "The Elderly Sick" (Aug. 6, p. 324) might have been more complete had it contained a warning against letting the pendulum swing too far in the direction of over-treatment of the aged. With ever-increasing lay participation in medicine, with "health" visiting, mobile physiotherapy, voluntary car pools, etc., there is, I submit, a grave danger that all sense of proportion may be lost. You speak of co-operation between G.P. and social services, lay-controlled. Do you, I wonder, realize the difficulty in which a G.P. may find himself should he try to do his duty by curbing their exuberant offers of help? As I write, a record harvest stands in stooks exposed to the risk of a break in the weather. A handful of men are struggling to get it in, but the towns and villages are thronged with people doing next to nothing. Let our professors of sociology come down from the sentimental clouds and bend their minds to the treatment of this besetting sin of our sickly civilization. Let our social reformers not make things too difficult for the young and vigorous among our people upon whom depends the bare survival of young and old alike.

### Antihistaminic Drugs for Burns

Dr. S. SHUBSACHS (Manchester) writes: While I agree with your correspondent Dr. Donnell Deeny (Aug. 6, p. 336) that it is logical to give an antihistaminic drug in burns, I must point out that the raised temperature is more likely to be due to other conditions, such as sepsis or heatstroke, than histamine excess. It is true that elevation of skin temperature 1° or 2° F. (0.6°–1.2° C.) can occur after the injection of small doses of histamine, as pointed out by Samson Wright (*Applied Physiology*, 1945, p. 556). But major burns are usually associated with normal or subnormal temperature, a rise in temperature only occurring after sepsis has set in. On the other hand, heatstroke can occur with minimal liberation of histamine in the skin. If the use of an antihistamine in burns leads to neglect of the significance of a raised temperature, then tragedies will occur and a valuable aid in the treatment of burns be unfairly discredited.

### Tuberculosis in Scotland

Dr. B. C. SAALER (London, N.W.11) writes: May I draw your and Mr. Walter Elliot's attention to a book by Fliess entitled *Vom Leben und vom Tod* (Jena, 1909), which I am afraid has not been translated into English? Discussing the tuberculosis mortality rates for Prussia, he warns the reader not to expect the curve always to move as it would if it depended on external factors only. According to him a nation is a biological unit and its life process is controlled by internal factors. Life is lived in waves; there are "high and low tides," mortality being low at low tides and increasing with the rising tide. He supports these views with evidence derived from knowledge he obtained through the study of the time factor in the life history of generations of human beings, animals, and plants, correlating all major events not due, or due not solely, to external influences. . . . A few questions raised by Mr. Elliot (Aug. 6, p. 297) point indeed to the possibility of an internal factor being responsible for the rise in the curve of the Scottish pulmonary tuberculosis mortality rate. What is affecting Glasgow which is not affecting Birmingham and Cardiff would be easy to see. The inhabitants belong to different biological groups. In England the "slope to the north" would become intelligible, and, as regards the different trend in the more agricultural counties of Northumberland and Cumberland, one could think of a greater reluctance of a peasant population to intermarry with city-bred people in Scotland, who, according to the figures given by Mr. Elliot, are in the main affected by the higher tuberculosis mortality rate. . . .

# Obituary

## Sir ALAN NEWTON, M.S., F.R.C.S., F.R.A.C.S. F.A.C.S.

Sir Gordon Gordon-Taylor and Professor C. Lambert Rogers write: The moving tributes (Aug. 20, p. 440) to the late Sir Alan Newton leave little for other friends to add, but perhaps further reference may be made to his enduring and passionate desire to promote the science and art of surgery in Australasia, and to ensure that the Cinderella sister college, in the inception and nurture of which he had played so important a role, should in all its activities be not unworthy of the Royal College of Surgeons of England with all its great tradition. Emphasis may be laid on the dignity and decorum on which he insisted in connexion with all the examinations held in the buildings of the Royal Australasian College of Surgeons. As Censor-in-chief he organized and himself superintended a primary fellowship examination in 1934, in which one of us (G. G.-T.) was privileged to participate: nothing was left undone, nothing omitted, nothing unanticipated, so that the examination might be conducted in the best tradition of Queen's Square and Lincoln's Inn Fields. To this end he gave up all his own work for a week and never left the building in Spring Street, Melbourne, during the hours of the examination. With princely courtesy, but with unmistakable firmness, it was impressed on the visitors from the English College of Surgeons that they were in Melbourne to conduct an important examination and not for their own enjoyment, and the mildest *divertissement* in which they might indulge had perforce to be kept from his ears. He would certainly have frowned had he known the late hours at the card-table in the club kept by the distinguished examiner in physiology, although he was well aware that the Royal College of Surgeons of England never had a better ambassador than George Buckmaster. As an examiner himself he was feared but respected.

As long ago as 1945 one of us (L. R.), speaking at the annual meeting of the Royal Australasian College of Surgeons, envisaged a day when there might be an interchange of examiners between the Mother Country and the Commonwealth, a dream that has recently been realized in the active part played by Professor Sunderland in a recent primary examination in London, but the official recognition of the Australasian primary fellowship by the English College, which Sir Alan had for so long regarded as a "statesmanlike desideratum," evoked in his breast the liveliest satisfaction. As alumni of Middlesex Hospital, we are both proud that he too learned anatomy within our walls, and still remember how 30 years ago a tall upright figure in the uniform of a major in the A.I.F. might have been seen striding into the dissecting-room of "Middlesex," along that floor which so many young surgical postgraduates from the lands under the Southern Cross have subsequently trod. As lecturer on surgical anatomy in the University of Melbourne doubtless he taught and retaught those lessons that he had learned as a disciple at the feet of "Tim" Yeates, whom he himself helped to discover and who remains so beloved a figure to Australian visitors of the third and fourth decades of the century.

It is curious that the motto of the Royal Melbourne Hospital which he served with such distinction and loyalty throughout his life should be the selfsame Virgilian line as that proudly possessed by the hospital in London which is our alma mater, and somewhere he himself has written that

"the secret of the care of the sick is to care for the sick." To this end he devoted his life unsparing of himself. Alan Newton was one who walked worthy of the vocation to which he was called, and had that gay, serene spirit which, as Schiller tells us, is the source of all that is noble and good.

Dr. ALBERT HOPKINSON died suddenly at his home in Cambridge on July 31 at the age of 85. The son of John Hopkinson, a former lord mayor of Manchester, he was educated privately and then at Owens College. In 1881 he came up to Emmanuel College, Cambridge, where he took his M.A. and M.B. degrees in 1889. He returned to Manchester and entered into general practice in Withington with the vigour and enthusiasm which were part of him. His especial love was the human aspect of practice, and he devoted himself with kindness, courtesy, and tireless energy to those under his care. It was during this period that he acquired the great human knowledge and sympathy which enabled him to influence the many medical students he taught in the latter part of his life. During the 1914–18 war Dr. Hopkinson was appointed medical officer to the Mosley Road Hospital, Manchester, which was devoted to the treatment of injuries to, and diseases of, the nervous system. "Here," Sir John Stopford wrote, "he worked tirelessly, not only clinically, but in encouraging the men. By his shrewd observation he did much to make possible the early investigations which greatly influenced the subsequent treatment of these diseases. His modesty made it impossible for him to realize the value of the work he was doing, but his colleagues and many of his patients have reason to be very grateful to him." In 1919 Dr. Hopkinson retired and came to live in Cambridge. At the invitation of his old college he undertook the supervision of medical students and became an assistant demonstrator in the school of anatomy, holding this appointment for nearly twenty years. Here he met and helped all the medical students who came to Cambridge during that period. The medical students in the materialistic world of the early 'twenties were apt to feel that they could ill afford the time to listen to his philosophic generalizations, and it was only in later years that they became fully appreciative of the lessons that he had taught them. It was a remarkable achievement to become a competent teacher of anatomy after half a lifetime in general practice, and only the possessor of an unusually retentive memory could have succeeded. In his teaching Hopkinson always made a point of emphasizing the applications of anatomy in practice. Patient and painstaking, he took a keen personal interest in the undergraduates, many of whom kept in touch with him long after they had gone down. Nor did he forget the subjects in the dissecting room, for he wrote a poem, a plea for their reverent handling, which was printed in the *Cambridge Review*. Hopkinson served on the advisory council of the Cambridge University Medical Society until after the recent war. The contact which this gave him with the rising generation of medical students was a constant joy, not only to him but to them. He was a life member of the British Red Cross Society. He also acted as treasurer for the Universities' Mission to Central Africa. As an undergraduate he represented his college at rugby football and athletics, and rowed in the college boat. All his life he was a keen mountaineer, and with his four brothers he was a member of the Alpine Club. In later years he took an especial interest in the Cambridge Mountaineering Club, and a more active one in the University Swimming Club, swimming a mile when he was close on seventy. His family life, despite the loss of one son in the first world war, was a very happy one until the death of his wife ten years ago. He is survived by two daughters and two sons, one of whom is in the medical profession. With the passing of Albert Hopkinson, Cambridge has lost a great and lovable personality who by his example has influenced the lives of many hundreds of medical men practising to-day.

Dr. DOUGLAS BELL died at his home at Skelmanthorpe on July 21 after a short illness. He was educated at the Watson Academy at Edinburgh, and graduated M.B., Ch.B. at Edinburgh University in 1904, taking the D.P.H. three years later. After a short period of assistantships he settled down in general practice with his brother, Dr. William Bell, at Skelmanthorpe, near Huddersfield. During the 1914–18 war he held a temporary commission in the Royal Navy and served in the flagship *H.M.S. King George V* at Jutland. He was for a time medical officer to the Royal Naval Barracks, Chatham. After the war he returned to general practice in Skelmanthorpe and was Medical Officer of Health to the Denby Dale Urban District from 1939 to 1945. He took a keen interest in all local activities; possessed of a strong personality, he was renowned for his forthright manner and his intolerance of petty officialdom. The personal and intimate family history of his patients was an open book to him, and he was an outstanding example of the old type of family doctor giving unstinted service to the community. His practice was his all-absorbing interest. It was his wish to die in harness, and it was fulfilled. He is survived by his wife and his son, Dr. Ian Bell, to whom the sincere sympathy of his colleagues and friends will be extended.

Mr. JOHN ROBERT FOSTER died at Danby on Aug. 5. Born at Sleights, Yorkshire, in 1868, he graduated at Edinburgh University in 1893 and took the F.R.C.S.Ed. in 1901. After holding house appointments at the Central London Ophthalmic Hospital, the Royal Westminster Ophthalmic Hospital, and the Royal National Throat, Nose, and Ear Hospital, Golden Square, he was appointed ophthalmic surgeon to the Hartlepools Hospital. A year later he was appointed ophthalmic surgeon to the Cameron and Howbeck House Hospitals and aural and ophthalmic surgeon to the Hartlepools Education Authority. He was an excellent and careful surgeon, and continued work until the age of 64, when he had to retire from hospital and private practice owing to ill-health. He is survived by a widow and three children, the eldest of whom is ophthalmic surgeon to the General Infirmary at Leeds.

Dr. ALEXANDER GORDON LEGGAT, who had practised in Newbury for nearly 30 years, died at Wellington, New Zealand, on Aug. 8. Dr. Leggat was born in Glasgow, and graduated at Glasgow University in 1905. In the 1914–18 war he served as major in the R.A.M.C. at Gallipoli and was awarded the D.S.O. He was a conscientious and able practitioner, and in 1931 was appointed to the staff of Newbury District Hospital. It was then that he found work most congenial to his taste and capacity, for he was a born administrator and took the greatest interest in the administration of the hospital. He was a firm but popular chairman, and kept order with a tact and humour which owed something to his Scottish origin. He will be greatly missed for his work at the hospital and his other activities. Dr. Leggat died as far from Newbury as it is possible to be on this planet, but near and dear to many of the inhabitants of the town. He survived the death of his wife by six months, and leaves a son and a daughter.

# Medico-Legal

## OVERDOSE OF NITROUS OXIDE

At an inquest held in Dublin on May 31 the jury found that the death of a woman of 38 was due to anoxaemia and cardiac failure following an overdose of nitrous oxide.

This patient had a septic left thumb which required incision. A woman house-surgeon at the Adelaide Hospital said that she had examined the patient and thought she was fit to be given an anaesthetic. She then noticed that the oxygen cylinder in the anaesthetic machine was empty. She asked one of the nurses to get a cylinder of oxygen and this was connected up; she turned on the nitrous oxide fully and the "oxygen" partially. After a few inspirations she noticed that the patient was becoming slightly blue. She therefore turned off the nitrous oxide and turned on the "oxygen." The cyanosis

became even more marked. She then examined the gas cylinders and found that both contained nitrous oxide. An oxygen cylinder was then put in and artificial respiration started. For two hours everything possible was done to revive the patient. She agreed that, though the cylinders were the same size, nitrous oxide cylinders had a black distinguishing mark and oxygen cylinders black with a white ring round the top. With continued usage the distinguishing white paint did tend to become worn.

A nurse described how she had brought into the theatre what she thought was a cylinder of oxygen. She did not examine the label on the cylinder to see whether it contained oxygen or not. The labels on the cylinders of nitrous oxide and oxygen were similar in size and she had no reason to believe that this cylinder did not contain oxygen. Later one of the medical students noticed that both cylinders in the anaesthetic machine contained nitrous oxide. She agreed that though the labels on the cylinders were of the same size they were of different colours. She had not seen gas cylinders being changed before in the course of her training and she had never been told of the distinguishing marks.

A fourth-year medical student said that he had been in the theatre for about five minutes, helping to apply artificial respiration, before he noticed that both cylinders in the anaesthetic machine contained nitrous oxide. He identified the cylinders by the labels. He did not look particularly at the tops of the cylinders.

The senior anaesthetist at the Adelaide Hospital described the methods of resuscitation employed and said that in her opinion death was due to anoxaemia and cardiac failure. Doctors were taught the importance of distinguishing between the colours of cylinders, but she thought that it would be better if the fittings were so arranged that it would be impossible to connect them up wrongly.

The manager of the firm which supplied the cylinders said that they were painted every two years.

The jury gave a verdict in accordance with the evidence and added a rider expressing the opinion that the Adelaide Hospital was guilty of negligence and that there was contributory negligence on the part of the house-surgeon.

# Universities and Colleges

## UNIVERSITY OF LONDON

The recognition of the British Postgraduate Medical Federation as a school of the University has been extended in respect of its facilities (*a*) at the Institute of Child Health and (*b*) at the Institute of Ophthalmology for three years and five years respectively in the first instance, from Oct. 1, 1948.

Sir Archibald Gray and Mr. J. B. Hunter have been appointed representatives at the University on the governing body of the British Postgraduate Medical Federation and Dr. Audrey Z. Baker representative on the governing body of Nonsuch County School for Girls, Cheam, Surrey.

A further A. H. Bygott Scholarship for 1949–50 (see *Journal*, Aug. 13, p. 393) has been awarded to Wilfred Charles Turner, M.B., B.S.

The Sir William Dunn Scholarship of the value of £100 for one year, which is awarded annually on the results of the second examination for medical degrees (internal and external) held in March, has been awarded, for 1949, to Charles John Edmonds (University College), who proposes to proceed to the B.Sc. (Special) degree in physiology.

Awards of medical entrance scholarships and exhibitions have been made on the results of the London Inter-Collegiate Scholarships Board examination, as follows: *Medical Scholarship*, Miss M. A. Clark (University College). *Bucknill Scholarship*, D. B. Thomas (University College). *Medical Exhibition*, R. Radford (University College). *Sambrooke Scholarship*, R. Conroy (King's College). *Mrs. George M. Smith Scholarship*, Miss M. Y. K. Armstrong (Royal Free Hospital School of Medicine). *Mabel Sharman-Crawford Scholarship*, Miss K. M. Barber (Royal Free Hospital School of Medicine).

# INFECTIOUS DISEASES AND VITAL STATISTICS

We print below a summary of Infectious Diseases and Vital Statistics in the British Isles during the week ended Aug. 6. [No. 31

Figures of Principal Notifiable Diseases for the week and those for the corresponding week last year, for: (a) England and Wales (London included). (b) London (administrative county). (c) Scotland. (d) Eire. (e) Northern Ireland.

*Figures of Births and Deaths, and of Deaths recorded under each infectious disease, are for:* (a) The 126 great towns in England and Wales (including London). (b) London (administrative county). (c) The 16 principal towns in Scotland. (d) The 13 principal towns in Eire. (e) The 10 principal towns in Northern Ireland.

A dash — denotes no cases; a blank space denotes disease not notifiable or no return available.

| Disease | 1948 (a) | (b) | (c) | (d) | (e) | 1947 (Corresponding Week) (a) | (b) | (c) | (d) | (e) |
|---|---|---|---|---|---|---|---|---|---|---|
| Cerebrospinal fever | 19 | — | 18 | 3 | — | 40 | 2 | 20 | 3 | — |
| Deaths | | — | 1 | | | | 3 | — | | |
| Diphtheria | 89 | 7 | 26 | 2 | 3 | 107 | 13 | 28 | 6 | — |
| Deaths | 1 | — | — | — | — | 1 | — | — | | — |
| Dysentery | 45 | 5 | 81 | — | 1 | 111 | 12 | 30 | — | — |
| Deaths | | | | — | — | | | | | — |
| Encephalitis lethargica, acute | — | — | — | 1 | — | — | — | 2 | — | — |
| Deaths | | — | | | | | 1 | | | |
| Erysipelas | | | 11 | 8 | 6 | | | 24 | 4 | — |
| Deaths | | — | | | | | — | | | |
| Infective enteritis or diarrhoea under 2 years | | | | 92 | | | | | 43 | |
| Deaths | 21 | 4 | 4 | 5 | 1 | 23 | 3 | 8 | 1 | 1 |
| Measles* | 3,683 | 273 | 71 | 121 | 66 | 6,879 | 430 | 52 | 46 | 42 |
| Deaths | | | — | — | — | | | — | | — |
| Ophthalmia neonatorum | 26 | 2 | 8 | — | — | 44 | 5 | 11 | — | — |
| Deaths | | | | | | | | | | |
| Paratyphoid fever | 37 | 1 | 1(B) | 2(B) | 1(B) | 47 | 3 | 3(B) | — | — |
| Deaths | — | — | — | — | — | — | — | — | | — |
| Pneumonia, influenzal | 220 | 15 | 2 | 2 | — | 363 | 26 | 1 | 2 | 1 |
| Deaths (from influenza)‡ | 4 | — | 1 | — | — | 6 | 2 | — | | — |
| Pneumonia, primary | | | 103 | 14 | | | | 113 | 21 | |
| Deaths | 94 | 16 | | 2 | 5 | 116 | 17 | | | 6 |
| Polio-encephalitis, acute | 22 | 2 | | | | 5 | 1 | | | |
| Deaths | | | | | | | | | | |
| Poliomyelitis, acute | 164 | 29 | 10 | 3 | — | 38 | 3 | 4 | 2 | 5 |
| Deaths§ | 12 | 1 | | | | | 4 | | | |
| Puerperal fever | | — | 6 | | | | — | 10 | | — |
| Deaths | | | | | | | | | | |
| Puerperal pyrexia‖ | 78 | 6 | 12 | — | — | 135 | 10 | 7 | — | — |
| Deaths | | — | | | | | 1 | | | |
| Relapsing fever | — | — | | | — | — | — | | | — |
| Scarlet fever | 854 | 45 | 134 | 41 | 28 | 848 | 49 | 134 | 29 | 21 |
| Deaths† | | | — | 1 | — | | | — | | — |
| Smallpox | — | — | — | — | — | — | — | — | — | — |
| Deaths | | | | — | — | | | | — | — |
| Typhoid fever | 5 | — | 1 | 9 | 2 | 10 | — | — | 4 | — |
| Deaths | — | — | — | — | — | — | — | — | — | — |
| Typhus fever | — | — | — | — | — | — | — | — | — | — |
| Deaths | | | | — | — | | | | — | — |
| Whooping-cough* | 1,566 | 74 | 43 | 67 | 85 | 3,185 | 263 | 11 | 79 | 12 |
| Deaths | 4 | — | — | — | — | 6 | 1 | 1 | | — |
| Deaths (0–1 year) Infant mortality rate (per 1,000 live births) | 198 | 31 | 29 | 11 | 6 | 247 | 41 | 40 | | 9 |
| Deaths (excluding still-births) | 3,632 | 563 | 465 | 135 | 103 | 3,586 | 584 | 517 | | 84 |
| Annual death rate (per 1,000 persons living) | | | 9·3 | 8·4 | | | | 10·4 | | |
| Live births | 7,121 | 1161 | 868 | 356 | 219 | 7,586 | 1242 | 939 | | 242 |
| Annual rate per 1,000 persons living | | | 17·4 | 22·1 | | | | 19·0 | | |
| Stillbirths | 169 | 24 | 20 | | | 161 | 19 | 31 | | |
| Rate per 1,000 total births (including stillborn) | | | 23 | | | | | 32 | | |

* Measles and whooping-cough are not notifiable in Scotland, and the returns are therefore an approximation only.

† Deaths from measles and scarlet fever for England and Wales, London (administrative county), will no longer be published.

‡ Includes primary form for England and Wales, London (administrative county), and Northern Ireland.

§ The number of deaths from poliomyelitis and polio-encephalitis for England and Wales, London (administrative county), are combined.

‖ Includes puerperal fever for England and Wales and Eire.

## EPIDEMIOLOGICAL NOTES

### Poliomyelitis

In the week ended Aug. 13 notifications in England and Wales were: poliomyelitis 236 (164), polio-encephalitis 18 (22). Figures for the previous week are shown in parentheses.

Counties with multiple cases (poliomyelitis and polio-encephalitis together) were: London 30 (31), Bedford 2 (5), Berkshire 2 (3), Buckingham 2 (1), Cambridge 2 (0), Chester 3 (3), Cornwall 6 (9), Devon 9 (6), Dorset 2 (1), Durham 3 (1), Essex 19 (7), Gloucester 7 (5), Hereford 4 (0), Kent 6 (3), Lancs 23 (12), Leicester 4 (5), Middlesex 10 (15), Norfolk 3 (0), Northampton 2 (0), Northumberland 4 (1), Nottingham 4 (1), Somerset 4 (2), Southampton 13 (9), Stafford 4 (2), Surrey 7 (7), East Sussex 5 (2), West Sussex 4 (2), Warwick 10 (5), Wiltshire 2 (2), Yorks East Riding 2 (2), Yorks West Riding 34 (17), Glamorgan 3 (5), Monmouth 4 (2).

Total notifications in the corresponding week of 1947 were: poliomyelitis 568, polio-encephalitis 56.

### Discussion of Table

In *England and Wales* there were decreases in the notifications of measles 583, whooping-cough 229, scarlet fever 191, dysentery 49, and acute pneumonia 43, with an increase in the incidence of acute poliomyelitis 17.

The largest falls in the notifications of measles were Durham 55, Sussex 44, Oxfordshire 42, Gloucestershire 42, and Yorkshire West Riding 41; the largest rise in incidence was Warwickshire 65. Notifications of whooping-cough decreased in Lancashire 52 and Essex 30, but rose in Warwickshire 42. The incidence of scarlet fever decreased in London 46 and in Yorkshire West Riding 36. No appreciable changes were reported in the notifications of diphtheria.

A further 4 cases of dysentery have been reported from the outbreak in Warwickshire, Warwick R.D. No further cases of dysentery have been notified from the outbreak in Buckinghamshire, Amersham R.D. There were 16 notifications of dysentery in Lancashire.

Notifications of food-poisoning numbered 356, an increase of 175 on the previous week. The largest notifications were Lancashire 131: Bury C.B. 43, Farnworth M.B. 43, Lytham St. Anne's M.B. 20; Yorkshire East Riding 54: Kingston-upon-Hull C.B. 54; Yorkshire West Riding 30: Sheffield C.B. 20.

In *Scotland* there were increases in the notifications of dysentery 41, scarlet fever 22, and paratyphoid fever 9. The increase in the incidence of dysentery was mainly contributed by Glasgow, where notifications rose from 14 to 59. Of the 10 cases of paratyphoid 8 were notified in Glasgow.

In *Eire* there were decreases in the notifications of whooping-cough 43, measles 24, and scarlet fever 18. There was an increase of 20 in the notifications of diarrhoea and enteritis in Dublin C.B.

In *Northern Ireland* a decrease of 19 in the notifications of measles was the only notable change in the trends of infectious diseases.

### Week Ending August 13

Notifications of infectious diseases in England and Wales during the week included: scarlet fever 689, whooping-cough 1,738, diphtheria 78, measles 3,226, acute pneumonia 227, cerebrospinal fever 26, acute poliomyelitis 236, acute polio-encephalitis 18, dysentery 62, paratyphoid fever 26, typhoid fever 11.

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When a death grant is payable under the National Insurance Act the cost of a hospital patient's burial arranged by a hospital management committee or board of governors will be met, up to a maximum of three-fifths of the grant, out of the National Insurance Fund. Formerly the maximum was one-half of the grant.

# Medical News

### Medical Research Council Travelling Awards

The Medical Research Council announces that it has made the following travelling awards for the academic year 1949–50: *Rockefeller Travelling Fellowships in Medicine.*—Mr. W. J. Atkinson, Mackenzie Mackinnon Research Fellow (Royal College of Surgeons), National Hospital, Queen Square, London; Dr. Ruth E. M. Bowden, Lecturer in Anatomy, Royal Free Hospital School of Medicine, London; Dr. R. Daley, First Assistant, Cardiology Department, St. Thomas's Hospital, London; Dr. J. Dawson, Lecturer in Biochemistry, University of Leeds; Dr. C. E. Lumsden, Senior Lecturer in Pathology, University of Aberdeen; Dr. J. S. Robson, Assistant, Departments of Medicine and Clinical Biochemistry, University of Edinburgh. *Dorothy Temple Cross Research Travelling Fellowships in Tuberculosis.*—Dr. A. J. Robertson, Medical Registrar, Royal Infirmary, Liverpool; Mr. J. D. Wade, Surgical Officer, Welsh National Memorial Association (Sully Chest Centre). *Travelling Scholarships under an exchange arrangement with the Centre National de la Recherche Scientifique in France.*—Dr. E. J. Field, Lecturer in Anatomy, University of Bristol; Miss A. M. N. Sewell, Nuffield Research Unit, Psychological Laboratory, University of Cambridge.

### American Committee to Study Rheumatism

Dr. Philip Hench, of the Mayo Clinic, has been appointed chairman of a committee in the U.S.A. to study new methods promising to alleviate rheumatic diseases. The other members are Dr. Walter Bauer, of Boston, Mass., General Hospital; Dr. Granville Bennett, of the University of Illinois School of Medicine; Dr. Jerome W. Conn, of the University of Michigan; Dr. W. Paul Holbrook, of Tucson, Arizona; Dr. Robert Loeb, of New York; Dr. Fred Moore, of the University of Southern California School of Medicine; Dr. Jane A. Russell, of Yale University School of Medicine; Dr. Emil L. Smith, of the University of Utah School of Medicine; and Dr. Alfred L. Wilds, professor of chemistry, University of Wisconsin.

### New Journal for Radiologists

The first issue of the *Journal of the Faculty of Radiologists* has just been published. All branches of radiology have expanded so rapidly in recent years that the Faculty of Radiologists felt that the time was opportune for the publication of a journal devoted to clinical radiology. This first issue includes a number of papers on cerebral tumour which were read at the annual meeting of the Faculty, and there are also articles on pneumoconiosis, on the radiotherapy of leukaemia, and on the doctor–patient relationship in the treatment of cancer. Inquiries should be addressed to the editor at the Faculty of Radiologists, 45, Lincoln's Inn Fields, London, W.C.2.

### Bristol Hospitals Fund

Since July 4, 1948, the Bristol Hospitals Fund has allocated £7,495 to hospital amenities funds, medical charities, and for medical research.

### Statistics in Israel

A new publication entited the *Statistical Bulletin of Israel* has been issued by the Israel Central Bureau of Statistics. Various statistics are given for cases of infectious diseases; the figures are fairly complete for the years 1936 to 1947, and figures for the Jewish population are given for 1948 in most cases.

### National Association for the Prevention of Tuberculosis

A scholarship of £300 offered by the association to enable a matron from a British sanatorium to spend three months visiting tuberculosis institutions in Canada has been awarded to Miss Nora Burrows, matron of Baguley Sanatorium, near Manchester. It is hoped that a matron from a Canadian sanatorium will pay a similar visit to this country.

### Visits Abroad of Ophthalmologists

During May nineteen ophthalmologists went to Italy on a tour organized by the Faculty of Ophthalmologists. At Pavia the rector of the university received them, and Professor Bietti gave some interesting talks and performed some operations. At Genoa Professor Maggiore showed the party round, and demonstrated some new instruments and some experiments in colour vision. The party then visited Professor Alajmo's clinic at Florence, where they saw some operations performed, including sclerectomy for glaucoma. Next day they went to Rome, where Professor Cavara showed some interesting cases, including one of "crocodile tears," and a hydatid cyst causing retinal detachment. Professor Leonardi in another hospital demonstrated cases of cataract extraction by suction apparatus. On reaching Naples the party was entertained by Professor Lo Cascio, who performed nine cataract extractions in 45 minutes. Finally the party went to Bologna and visited Professor Di Marzio's clinic, where papers were read on pituitary tumours and nasal infection in eye diseases. In June twenty members of the Faculty, under the leadership of Mr. W. Muirhead (Sheffield), were received by the heads of the ophthalmic clinics at Copenhagen, Lund, Uppsala, Stockholm, Oslo, and Gothenburg. Lectures, clinical demonstrations, and operative sessions were arranged, and the tourists were made welcome in the homes of their Scandinavian friends.

### Hospital Contributory Schemes

A history of the British Hospitals Contributory Schemes Association will be published in the autumn under the title *Pennies for Health*. The cost will be 13s. 3d. post free, and orders may be sent to the British Hospitals Contributory Schemes Association (1948), Royal London House, Queen Charlotte Street, Bristol, 1.

### Faculty of Radiologists

At the recent annual general meeting of the Faculty of Radiologists the following officers were appointed for 1949–50. President: Professor B. W. Windeyer, London. Vice-presidents: Dr. J. L. A. Grout, Sheffield (Diagnosis); Dr. J. R. Nuttall, Leeds (Therapy). Warden of the Fellowship: Dr. S. Cochrane Shanks, London. Editor: Dr. Peter Kerley, London. Hon. treasurer: Dr. J. W. McLaren, London. Hon. secretary: Dr. E. Rohan Williams, London.

### Nuffield Orthopaedic Centre

Lord Nuffield has made a further gift to the Nuffield Orthopaedic Centre at Oxford. The donation is of £50,000, and the fund will be used mainly to offer special facilities for visiting orthopaedic specialists and students from the Commonwealth. The gift is comparable to Lord Nuffield's recent benefaction to the Royal College of Surgeons of England.

### Medical Films

The following medical films are available on request from the Documentary Film Unit, May & Baker, Ltd., Dagenham: "Thiopentone Sodium and its Use in Intravenous Anaesthesia" (made in co-operation with the Department of Anaesthetics, Westminster Hospital, London); running time is 38 minutes on 16 mm. and 35 mm. (with sound track). "Medical Applications of Sulphonamides"; running time is 34 minutes on 16 mm. and 35 mm. (with sound track). Both films are divided into three sections—namely Introduction (chemistry), Pharmacology, and Clinical Use. Applicants should specify alternative dates when possible. Synopses may also be obtained.

### Wills

Professor Stuart McDonald, who was emeritus professor of pathology in Durham University, left £7,933. Dr. Lionel James Picton, of Holmes Chapel, Cheshire, left £15,308. Mr. Robert Leslie Dodds, of London, N.W., left £2,195. Dr. Howard Bluntisham Hodson, of Colchester, left £8,596. Dr. Oswald Hanson Isard, of Tonbridge, Kent, left £59,739, including £100 to the Royal Medical Benevolent Fund.

## COMING EVENTS

### South-east Metropolitan Regional Tuberculosis Society

A meeting of the South-east Metropolitan Regional Tuberculosis Society will be held at B.M.A. House, Tavistock Square, London, W.C., on Saturday, Sept. 10, at 10.30 a.m., when a lecture on "The Secondary Effects of Tuberculous Mediastinal Lymphadenitis, with Special Reference to Disease of the Middle Lobe" will be delivered by Mr. R. C. Brock. The meeting will be followed by the annual luncheon of the society at Russell Hotel, Russell Square, London, W.C.

### Rehabilitation Clinic

A special clinic on rehabilitation will be held by Dr. Howard Rusk, of New York, at the Royal Free Hospital, Gray's Inn Road, London, W.C., on Wednesday, Sept. 14, at 2.30 p.m., when Dr. Rusk will demonstrate his special methods of approach to the subject. The chair will be taken by Lord Horder. Anyone who wishes to be present should notify the Medical Rehabilitation Unit at the hospital.

### Association of Army Psychiatrists

The seventh reunion of army psychiatrists will take place at Slater's Restaurant, 18–24, High Street, Kensington, London, W., on Saturday, Sept. 24, from 7.30 to 10.30 p.m. Particulars may be obtained from the honorary secretary, Dr. J. C. Penton, The Old Farm House, 1, Gatehill Road, Northwood, Middlesex.

### Lectures in Social Studies

The Institute for the Scientific Treatment of Delinquency (8, Bourdon Street, Davies Street, London, W.1) announces the following university extension lectures for candidates for the Diploma in Social Studies. Twelve lectures on "Criminology," by Mr. H. Mannheim, on Tuesdays, at 6.30 p.m., beginning on Sept. 27; 24 lectures on "Social Philosophy," by Mr. J. J. Hartland-Swann, Ph.D., on Wednesdays, at 6.30 p.m., beginning on Sept. 28; 24 lectures on "Social Psychology," by Mr. R. Elias, Dr.Phil., on Thursdays, at 6.30 p.m., beginning on Sept. 29; 24 lectures on "Social Structure," by Mr. B. C. Adams, on Fridays, at 6.30 p.m., beginning on Sept. 30; 12 lectures on "The Psychology of Delinquency," by Dr. Edward Glover, on Tuesdays, at 6.30 p.m., beginning on Jan. 10, 1950. The lectures are open to members and non-members of the institute and to diploma and non-diploma students. As each class will be limited in number early application for enrolment forms should be made to the education secretary of the institute at the above address. The fee for 24 lectures is £1 10s., and for 12 lectures 15s.

### French Medical Congress

The Association des Médecins de Langue Française will hold a congress at Geneva on Sept. 29–Oct. 1. Subjects to be discussed include plasma proteins, hyperthyroidism, and hormone treatment of cancer. Information may be obtained from Professor E. Martin, 16, Boulevard Helvétique, Geneva.

### Course on Rheumatic Diseases

A concentrated week-end course on the rheumatic diseases, with lectures, ward-rounds, and practical demonstrations, will be given at the Rheumatism Unit, St. Stephen's Hospital, London, S.W., on Oct. 1 and 2. The course will be opened by Sir Ernest Rock Carling with an address on "Some Social and Economic Aspects of the Chronic Rheumatic Diseases." Other lecturers will include, Dr. Francis Bach, Dr. Grace Batten, Dr. Philip Ellman, Mr. Timbrell Fisher, Dr. Jackson Richmond, Dr. David Shaw, Dr. A. G. Signy, and Dr. Worster-Drought. Applications to attend the course should be made to the medical registrar, Rheumatism Unit, St. Stephen's Hospital, London, S.W.10, or to the Fellowship of Postgraduate Medicine, 1, Wimpole Street, London, W.1.

### Safety in Chemical Works

The Association of British Chemical Manufacturers has arranged to hold a conference on "Safety in Chemical Works" on Oct. 7 to 9 at Scarborough.

### French Dental Congress

The annual congress of the Confédération Nationale des Syndicats Dentaires will be held on Oct. 3–9 in Paris. Visitors from abroad are invited, and further information may be obtained from the secretary of the congress at 31, Rue Tronchet, Paris, 8e.

### International Society of Medical Hydrology

The annual meeting of the International Society of Medical Hydrology will be held at Dax, Landes, France, from Oct. 9 to 15. Further particulars may be obtained on application to the honorary secretary, Dr. Donald Wilson, "Cranbourne," Southdown Road, Bognor Regis, Sussex.

## SOCIETIES AND LECTURES

**Monday**

EDINBURGH POSTGRADUATE BOARD FOR MEDICINE.—At Anatomy Lecture Theatre, Edinburgh University, Aug. 29, 4.30 p.m., "*Influenza in Perspective*," by Dr. C. H. Andrewes, F.R.S.

## APPOINTMENTS

MACDOUGALL, IVOR ANDERSON, M.B.E., M.R.C.S., L.R.C.P., D.P.H., Medical Officer of Health and School Medical Officer to the County Borough of Bournemouth. (From Feb. 26, 1950.)

PRIESTMAN, AUSTIN, M.B., Ch.B., D.P.H., Temporary Medical Officer of Health, Borough of Richmond and Rural Districts of Richmond, Croft, and Startforth, Yorkshire.

## BIRTHS, MARRIAGES, AND DEATHS

### BIRTHS

**Galewski.**—On August 11, 1949, at Queen Charlotte Maternity Hospital, London, to Anna (née Galin), wife of Dr. Galewski, a daughter.

**Rosenvinge.**—On August 5, 1949, at Carlton Lodge, Harrogate, to Margaret (née Ogden), wife of Dr. Gerald O. Rosenvinge, of 35, Hookstone Drive, Harrogate, a brother for Louise and Stephen—Henry Paul.

### MARRIAGE

**Marciniec—Macfarlane.**—On August 13, 1949, in London, Antoni Marciniec, Captain P.R.C., to Laura Helen Macfarlane, M.D., D.O.M.S.

### DEATHS

**Blampied.**—On August 15, 1949, at Seymour Cottage, La Rocque, Jersey, Harold John Blampied, M.B., B.S., aged 56.

**Chissell.**—On August 15, 1949, at Middlesex Hospital, Gordon Frank Chissell, M.R.C.S., L.R.C.P., aged 53.

**Gater.**—On August 10, 1949, at Brighton, Horace James Gater, L.M.S.S.A., of Santos, Little Crescent, Rottingdean, Sussex, formerly of Peckham.

**Green.**—On August 19, 1949, Philip Withers Green M.R.C.S., L.R.C.P., of 5, Cheyne Gardens, Chelsea, London, S.W.

**Hollings.**—On August 13, 1949, Guy Bertram Hollings, M.D., F.R.C.S.Ed., of Torrington House, Berkhamsted, Herts.

**Jackson-Taylor.**—On August 18, 1949, Basil John Francis Jackson-Taylor, M.R.C.S., L.R.C.P.

**Jameson.**—On August 20, 1949, at 95, Bouverie Road, Folkestone, Archibald Douglas Jameson, M.R.C.S., L.R.C.P., Lieutenant-Colonel, R.A.M.C., Ret., aged 71.

**Laidlaw.**—On August 9, 1949, at 109, Grantchester Meadows, Cambridge, Janet Young Laidlaw, M.B., B.S., aged 66.

**Leggat.**—On August 8, 1949, at Wellington, New Zealand, Alexander Gordon Leggat, D.S.O., T.D., M.B., Ch.B., D.P.H., of Monkswood, Newbury.

**Littlewood.**—On August 1, 1949, at "Highfields," Woodhouse Road, Mansfield, Samuel Littlewood, M.B., B.S., aged 64.

**Lyle.**—On August 2, 1949, at "Moyle," Belmont Road, Belfast, William Lyle, M.B., B.Ch., B.A.O., M.P., aged 78.

**Newfield.**—On August 13, 1949, at Buck's House, Great Bardfield, Essex, Maurice Newfield, M.R.C.S., L.R.C.P., aged 55.

**Owen.**—On August 19, 1949, at Royal White Hart Hotel, Beaconsfield, Daniel Stanley Owen, L.S.A., late of Langford House, Higham Hill, Walthamstow, London, E.

**Paterson.**—On August 2, 1949, George William Murray Paterson, F.R.C.S.Ed., of 84, Oswald Road, Scunthorpe, Lincs.

**Ramsay.**—On July 26, 1949, at Edinburgh, James McAlister Ramsay, L.R.C.P.&S.Ed., L.R.F.P.S.Glas., of 11, Brucehaven Crescent, Limekilns, Fife.

**Scott.**—On August 16, 1949, at Hill Crest, Sileby, Leics, Alexander Scott, M.B., Ch.B.

**Steven.**—On August 9, 1949, at "Ardglass," Lochgoilhead, George Henry Steven, M.B., Ch.B.

**Stone.**—On August 17, 1949, at Sedgewood, Vittoria Walk, Cheltenham, Charles Ainslie Stone, M.B., B.Ch., aged 70.

**Symons.**—On August 18, 1949, at 17, Boscombe Spa Road, Bournemouth, Annie Dorothea Symons, M.R.C.S., L.R.C.P.

**Warwick.**—On August 21, 1949, at the Middlesex Hospital, London, W., William Turner Warwick, F.R.C.S., of Fitzroy Farm Cottage, Highgate, London, N.

**White.**—On August 4, 1949, in Guernsey, Digby Ccoke White, M.D., aged 81.

**Whitelaw.**—On August 14, 1949, at Osborne House, Bathampton, Bath, James Charles Graham Whitelaw, M.B., B.Chir., aged 43.

**Willoughby.**—On August 13, 1949, at St. Bartholomew's Hospital, London, William George Willoughby, M.D., of 17, Hartfield Square, Eastbourne, aged 83.

**Wills.**—On July 30, 1949, at Bath, James Tremlett Wills, M.B., B.Ch., aged 78.

# Any Questions ?

*Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.*

### Hypertension and Pregnancy

**Q.**—*A married woman aged 26 is anxious to have another child if it is not likely to damage her health. During her first pregnancy, which ended in a live birth, she suffered from high blood pressure. In the 32nd week of her second pregnancy her blood pressure was 145/95 mm. Hg; there was oedema of the ankles but no albuminuria. At the 36th week she went into labour and was delivered of a stillborn child weighing 3 lb. (1,360 g.) and an unhealthy, small, infarcted placenta. There were no foetal abnormalities. Her blood pressure is now 135/85 mm., and there is no albuminuria. What advice should I give her about another pregnancy?*

**A.**—The history suggests a diagnosis of essential hypertension rather than a recurrent pre-eclamptic state, and this despite the fact that the blood pressure is not much raised at present. Is there any family history of vascular disease? If this diagnosis is correct, it seems likely that another pregnancy will also be complicated by an exacerbation of the hypertension and possibly by albuminuria in the later weeks. In such event there is also an appreciable chance that the woman might be left with a persistently raised blood pressure. Although it is not inevitable, the next foetus is likely to be poorly developed, and its live birth could not be guaranteed. These points should be put to the patient, but it is doubtful whether the risks are grave enough to justify advising her not to embark on another pregnancy. It would, however, be wise for her not to try to conceive until two years after the last confinement, and at that time estimations of blood pressure and renal function should be made. During the next pregnancy she should rest for regular periods each day and should be kept under the closest observation. A rise in blood pressure or the appearance of albumin in the urine would call for her admission to a well-equipped maternity hospital, and in the interest of both mother and child premature termination of pregnancy might be necessary. The method of termination could be decided according to the circumstances present at the time, but caesarean section under local analgesia has its place in some of these cases.

### Blood Circulation Time

**Q.**—*The fact that sodium dehydrocholate, when injected intravenously, gives rise to a bitter taste on the tongue has been utilized to determine the arm–tongue circulation time of the blood. The interval between the injection into a vein of the arm and the moment a bitter taste is experienced is generally reckoned to be from eleven to nineteen seconds. Over a similar distance—from a vein in the antecubital fossa to the olfactory nerve—by using a solution of sodium penicillin I have lately demonstrated a circulation time of eight seconds or less. Perhaps this is because the olfactory sense organ is more quickly stimulated. I should like to know wherein lies the flaw, as the figure arrived at by this method is only about half that generally accepted.*

**A.**—Determination of the circulation time, usually measured from the arm to the tongue, is a very complex affair. A high concentration of sodium dehydrocholate is produced in the veins of the arm into which the injection is made. This concentration, however, is considerably diluted in the great veins and in the right heart. Furthermore, rates of blood-flow through the different parts of the lung vary somewhat, and by the time the systemic arteries are reached the injected substance has been considerably diluted. The concentration in arterial blood begins to rise about the 9th to 12th second after injection, reaches a peak in 14 seconds, and thereafter

falls away more slowly. These phenomena have recently been well demonstrated by Prinzmetal and his colleagues (*J. Amer. med. Ass.*, 1949, **139**, 617) by following the passage of injected radioactive sodium through the right and left heart with a Geiger counter placed over the chest.

It is clear that sensory perception of the arrival of these diluted test substances is governed by the sensitivity of the sensory end-organs and by the reaction-time of the patient. Presumably the olfactory perception of sodium penicillin is sensitive to much greater dilutions of the substance, and the very beginning of a rising concentration may be recognized. Sodium dehydrocholate is recognized only some seconds later when a greater concentration reaches the taste buds in the tongue. Alternatively, substances perceived by sense of smell may diffuse through the lungs, reaching the nose in the expired air. This is the basis of the arm–lung circulation time with injected ether, which is, of course, much shorter than the arm–tongue time. Some of the prolongations of circulation time in heart failure are due to dilution of the test substance in the dilated heart and engorged lungs. The patient simply does not perceive the smaller concentrations reaching his tongue until the delayed peak of concentration is attained, after which the taste may last an unduly long time. Rapid injection of the test substance is of the utmost technical importance if any comparative value is to be placed on circulation times for clinical assessment.

### Jealousy in a Child

**Q.**—*I am the mother of two little boys. The elder, Peter, aged 4, is intensely jealous of the younger, Paul, aged 2½. The jealousy first appeared when Paul started to toddle and Peter constantly pushed him over. Now he hits him, teases him, refuses to let visitors speak to him, interrupts plans for little outings, etc., and screams and rages for anything that Paul is playing with. Paul in his early days was cared for mainly by my mother's help, as I was temporarily crippled and could not handle him. I tried to show Peter how much I loved him, and had him with me a good deal, but in order to achieve safety and peace for Paul I have often had to smack him. Paul is a shy, good-tempered, generous little boy. Peter gets on very well with other people and seems to have a charming personality, and I do want to help him to grow up well balanced. This temperament has appeared in older generations of the family, so I feel that it may be an inborn tendency rather than something that has arisen as a result of environment only. I would appreciate it if you could indicate a steady line of action.*

**A.**—The origin of Peter's extreme jealousy of Paul may well be connected with your prolonged disability. Although this had nothing to do with the latter's birth, it would certainly have appeared to the eighteen-months-old Paul as the work of the wicked baby who had damaged you and might do so again. It is quite possible that the word "jealousy" is out of place in this case, for, since the attacks on Paul did not start for about a year, it may be that Peter really wanted to like the new brother, and could do so as long as his inability to get about made him harmless. At the toddling stage, however, Paul's increased mobility would again make him appear as a danger against which you must be protected at all costs by the loyal Peter, who would then have been 2½ years old—a peak period in a child's attachment to his mother. This explanation, being in line with common fantasies of early childhood, is more likely to account for the trouble than can any theory of inborn tendency, especially as Peter has a charming personality otherwise. He is now at an age when companionship with his father might help by leading to adoption of the latter's attitude—"being like Daddy" towards Paul and yourself. Another suggestion is to tell Peter quite factually how your disability arose, making it clear that it had nothing to do with Paul. This might be followed by schemes in which you and he in partnership arrange things for Paul, so making him feel you are on his side, though obviously you must protect the younger son until there is a change of attitude, and this may take much time and patience. If these home measures do not succeed, as they may well do, it is likely that a fairly short period of child psychotherapy would be effective.

### Mild Thyrotoxicosis

**Q.**—*In a mild case of primary thyrotoxicosis in a female aged 30 there appear to be three ways of treatment: (1) with Lugol's iodine; (2) with methyl thiouracil; and (3) by subtotal thyroidectomy. Some cases are effectively controlled by Lugol's iodine continued indefinitely; if this treatment is not enough, can it be supplemented with methyl thiouracil? What is the current relationship between medical and surgical treatment of mild early cases in patients under 30?*

**A.**—Most authorities would contest the statement that thyrotoxicosis can be controlled indefinitely by Lugol's solution. It is common experience that iodine has a rapid and short-lived effect, which reaches a maximum about three weeks after its administration is started. The available effective methods of treatment are with methyl thiouracil, by operation, and with methyl thiouracil followed by operation. In a mild case in a young woman, prolonged treatment with methyl thiouracil in small doses is a reasonable choice. At this age the disease is often self-limiting, and after nine to twelve months it may be possible to withdraw the drug without consequent relapse. Operation is to be preferred if there is a large goitre, and particularly if it has a retrosternal prolongation, for it may increase in size after medication with thiouracil. Many prefer preliminary "detoxication" with thiouracil, followed by thyroidectomy. An interval of three weeks should elapse between discontinuing the drug and the operation, and during this period Lugol's solution should be given. By this step the vascularity of the gland is decreased and the technical difficulties of the operation are lessened. It cannot yet be said that the relative positions of surgery and methyl thiouracil in the treatment of thyrotoxicosis have been precisely defined.

### Acroparaesthesia

**Q.**—*A woman aged 44 has for three years complained of paraesthesia in the tips of her fingers, worse on the left than the right, and followed by a pain which spreads up the arms to the shoulders. These symptoms start when she gets warm in bed; the pain is worst after a day's washing. There are no abnormal physical signs: radial pulses are equal in rate and volume; sensation and reflexes are normal; there is no tenderness over the ulnar nerve; and the skin is normal in appearance. Please suggest diagnosis and treatment.*

**A.**—The condition as described is acroparaesthesia, which is fully discussed in textbooks. No physical signs are found when tingling is not present, but the hand is often red and puffy then. The condition is vascular, and is thought to be the same as release tingling.

### Excessive Salivation

**Q.**—*In a female aged 56 suffering from progressive motor neurone disease the most distressing symptom is loss of control of salivation; the saliva pours from her mouth in a constant stream. The following drugs have had little or no effect: tincture of belladonna, stramonium, hyoscine, tincture of opium, and nicotinic acid. Can anything else be done to control the salivation?*

**A.**—This symptom is a very difficult one to treat, because in most cases it is the failure of the patient to control the salivation which causes the trouble. We do not know of any other substance which can be used, but atropine alone, if given in large enough doses, is sure to reduce salivation.

### Sulphonamide Sensitivity

**Q.**—*A woman died of subacute necrosis of the liver as a result of sensitivity to sulphonamides. Is sensitivity to these drugs an inheritable factor, and is there a simple cutaneous test to determine such sensitivity?*

**A.**—There is no satisfactory skin test to determine sulphonamide sensitivity. Such sensitivity is not known to be inherited, and subacute necrosis of the liver, although sometimes attributed to the action of one of the sulphonamide drugs, is a rare and unusual sequel to their administration.

### Alopecia Totalis

**Q.**—*Eighteen months ago a healthy woman aged 35 observed a small bald patch behind the ear. In spite of treatment the condition spread to involve the occiput and rapidly progressed to alopecia totalis; a few lanugo hairs are visible on the body, but no pubic or axillary hair, eyelashes, or eyebrows exist. The patient continues to menstruate normally and her weight remains constant. The scalp has been painted with a preparation containing radon as well as with liquor iodi fortis, and the patient has been given injections of testosterone propionate, but all to no avail. Is the prognosis quite hopeless so far as regeneration of scalp hair is concerned?*

**A.**—The alopecia is, of course, symptomatic and there must be some underlying cause, probably psychogenic or endocrine, even though it is not apparent. It is important to know whether the patient had previously suffered from alopecia or whether there is any family history of the affection. Prognosis depends on the underlying cause. There is probably no destruction of follicles, so that theoretically hair may regrow, but in practice the prognosis is generally bad.

### Infection from Crockery

**Q.**—*Can you tell me if the use of glazed earthenware vessels may be detrimental to health owing to frequent crazing or fine cracking of the glaze allowing the entry of organisms? What is the risk in Britain, as compared with countries in the East?*

**A.**—Chipped and cracked cups, which are consequently impossible to clean, can convey bacteria from mouth to mouth and may therefore be concerned in transmitting throat and mouth infections, such as streptococcal sore throat and Vincent's angina; they have even been known to transmit syphilis. This does not apply to utensils used only in the kitchen, since there is no reason why they should become contaminated with pathogenic bacteria. The worst that bacteria in cracks in earthenware glaze are likely to do in ordinary circumstances is to cause the more rapid souring of milk. The same considerations would seem to apply in any country, except that in hot climates and without refrigeration bacterial growth would be more rapid.

### Chronic Intermittent Priapism

**Q.**—*A man of 42 recently suffered for a few days from pain in the groin, with maximum tenderness over the right pubic bone where the cord passes over it. There was no abnormality of the cord and no rupture; both testes were descended and not swollen or painful. There was, however, a partial erection of the penis, which was painful from congestion, and a small hard lump was palpable underneath at the root of the organ. The patient had been circumcised, but gave a history of penile eczema from infancy to the age of 25. The skin of the penis, though intact, is easily irritated by slight trauma. There have been occasional similar attacks for a year or two. His sexual life seems to be normal. Can you suggest any treatment?*

**A.**—Persistent erection of the penis occurs with thrombosis of the corpora cavernosa, which may be of unknown causation or associated with various disorders of the blood; it is a well-recognized complication of chronic myeloid leukaemia. Although the congestion of the organ raises suspicions of a thrombotic origin, the recurrent attacks make it improbable. A chronic intermittent priapism is known to occur; it is sometimes associated with lesions in the posterior urethra or prostate or with disease of the central nervous system. These aspects of the case require investigation. No cause can be found in other instances, and treatment is then unsatisfactory. Some relief has been obtained with heat applied by the diathermy current, and occasionally irradiation is effective. The palpable nodule at the root of the penis raises the possibility of fibrous cavernositis or plastic induration of the penis. Priapism is not a usual symptom in this condition, which is again resistant to treatment, although some success has followed injections of fibrolysin into the lesions.

### Sodium Glutamate

**Q.**—*What are the chemical and physical properties, physiological actions, method of manufacture, etc., of sodium glutamate?*

**A.**—Sodium glutamate is the sodium salt of glutamic acid—a simple amino-acid which occurs in food protein and as part of the molecule of folic acid. Its structure may be thought of as a compound of acetic acid and the amino-acid alanine. Alanine is $H–CH_2.CH.NH_2.COOH$, while acetic acid is $H–CH_2.COOH$. If H is removed from each substance and the residues are joined, the result is glutamic acid. Like other amino-acids, it has no physiological action. Its manufacture is indicated by the structure.

## NOTES AND COMMENTS

**Delirium Tremens.**—Dr. A. E. CARVER (Nuneaton) writes: I was shocked to read in answer to the question, "What is the best treatment for delirium tremens?" ("Any Questions?" July 23, p. 242), that small doses of alcohol plus intramuscular injections of 2 dr. (8 g.) of paraldehyde were recommended. Although D.T. is not now so common as it used to be in my young days, I did think that there was general agreement among those called upon to deal with it that once it was established alcohol should be immediately and completely cut off, since its exhibition has been found to prolong this brief psychosis. In long-standing topers, who alone are subject to D.T., a small quantity of alcohol is irritating, not soothing. Forty and more years ago there was an idea that D.T. was due to an excess of some hypothetical anti-alcohol substance in the body and that giving alcohol would neutralize this, but such an idea has long since been disproved. Healthy heavy drinkers sent to prison and abruptly cut off alcohol do not develop D.T. Some trauma or acute disease (e.g., broken leg or pneumonia) seems to be a necessary precipitating factor, and the welfare of the patient depends far more upon how this is attended to than upon the restless delirium, which usually is controllable by repeated small injections of hyoscine hydrobromide. Other sedatives and hot packs may also be employed, but intramuscular injections of paraldehyde should certainly be eschewed. I wonder whether he who answers the question has tried them.

**Sulphur-containing Sweat.**—Dr. J. N. MORRIS (Stoke, Plymouth) writes: In "Any Questions?" (July 16, p. 189) sulphur-containing sweat is discussed. I have known this condition to follow the taking of Epsom salts or other sulphur-containing laxatives. This may be the explanation in your correspondent's case.

Miss W. JOAN WADGE, F.R.C.S. (London, W.), writes: With reference to the question and answer under this heading ("Any Questions?" July 16, p. 189), I have seen this in patients who were applying a sulphur-containing liniment to the skin (elsewhere than on the hands). Bowel function was normal.

**Bee-stings.**—Dr. W. K. WENNER (Upper Montclair, New Jersey) writes: With regard to the question on bee-stings in the *Journal* (June 11, p. 1061), may I draw your attention to a paper by W. T. Strauss (*J. Amer. med. Ass.*, 1949, **140**, 603), who reports good results by topical application of the antihistamine "thephorin" (2-methyl-9-phenyl-2,3,4,9-tetrahydro-1-pyridindene hydrogen tartrate)?

**Anaesthetics for Domiciliary Midwifery.**—Dr. S. RANSOM (Obstetric Unit, University College Hospital, London, W.C.) writes: I am glad that Dr. J. E. M. Barnes (Aug. 6, p. 346) has drawn attention to the misleading statement that the Cyprane inhaler can produce anaesthesia. We in this department at any rate have not been able to use the apparatus for this purpose, though we found it satisfactory for producing analgesia.

All communications with regard to editorial business should be addressed to THE EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE, TAVISTOCK SQUARE, LONDON, W.C.1. TELEPHONE: EUSTON 2111. TELEGRAMS: *Aitiology, Westcent, London.* ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone unless the contrary be stated.

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